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ON THE PATHOGENESIS OF CARDIOSPASM

An Experimental Study

P. Alnor, Dr.Med., Kiel, Germany

INTRODUCTION

CERTAIN swallowing difficulties were described by Willis (1672) and later by Hoffmann (1733) and Purton (1821). In 1881, von Mikulicz gave the syndrome the name of "cardiospasm." Although it is now generally recognized that the condition is not associated with any true spasm, this name is still widely used. During the last few decades, numerous cases have been described, but the etiology and pathogenesis are not yet properly understood. In addition, it was not until recent years that general therapeutic principles began to emerge from the critical analyses and comparisons of the late results achieved by different types of treatment.

Although the condition is still commonly referred to as cardiospasm, the name achalasia, i.e., failure of the cardiac orifice to open after all the reflex movements of deglutition have come to an end, is far more correct and should be preferred. The clinical picture described by von Mikulicz is not associated with any spastic condition of the esophagus. Diffuse spasm of the esophagus is a separate clinical entity (Olsen and associates) and should not be confused with achalasia, although both conditions may be seen in association with one another. Spasm of the esophagus is accompanied by hypermotility, achalasia by hypomotility or even paralysis of the entire esophagus (Pupple). The contractions are often irregular, incoordinated and, as a rule, refractory to

From the Chirurgische Universitätsklinik, Kiel, Germany; Head Professor, Dr. R. Wanke.
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stimulation. One of the reasons why it is so difficult to understand the nature of the disease is that our knowledge is not sufficient to form a concise opinion of the normal anatomy and physiology of the cardia. Being a junctional region between the esophagus and the stomach, the cardia receives only little space in the anatomic literature. Several physiologic investigations on the act of deglutition and the function of the cardia are, however, on record, but owing to lack of agreement on several points it is also difficult to form more than a vague, general notion of the physiology of swallowing.

A clear concept of the normal anatomy and physiology of the cardia is necessary for investigation of the pathogenesis of achalasia. With this purpose in view we analyzed the literature in this field and carried out some personal experiments.

On the basis of these studies it appears that the lower end of the esophagus is not equipped with a sphincter muscle in the anatomic sense of the word. The cardiac orifice is normally held closed by a number of different factors, above all by the tone of the cardia and the slope of the esophagus as it joins the stomach with the formation of the plica cardiaca (Alnor, Robert and Hoffmann, Watkins and Prevedel, Kelling, Zaaijer, and others).

Of importance for the understanding of the pathogenesis of diseases of the cardia is knowledge of the physiology of deglutition. Via fibers given off by the vagus nerve and entering the esophagus above the level of the lung hilus the central nervous system sends a stimulus either along the intramural esophageal fibers or Auerbach's plexus and the smooth musculature with relaxation of the cardia as a consequence. Our investigations provided no support for the assumption of Knight and Lehmann that subsequent contraction is due to stimulation by the sympathetic nerve. We found that even division of all of the sympathetic fibers running to the cardia did not interfere with normal deglutition. In our opinion, it must be assumed that the neuromuscular system of the cardia is responsible for the contraction following relaxation. According to Cannon, this system permits local coordination or local automatism. This is also supported by the fact that vagotomy is followed by symptoms of achalasia which, however, gradually disappear.

The smooth musculature and Auerbach's plexus are thus essentially responsible for normal function of the cardia. Only if this neuromuscular system is intact can cardiac function be normal. Accordingly, the cause of the disturbance of cardiac function seen in achalasia should reasonably be sought in this system.

PATHOPHYSIOLOGY

The cardia serves two purposes: it is normally closed to prevent regurgitation of the stomach contents or acid gastric secretion and, second, it relaxes to permit the passage of food from the esophagus to the stomach. Therefore two types of disturbances may occur: lack of relaxation (achalasia) or imperfect closure with gastroesophageal reflux, sometimes with consequent esophagitis and subsequent complications such as hemorrhage, stenosis, ulcer formation, and perforation.

Numerous theories on the pathophysiology of achalasia, some based on more or less purely hypothetical grounds, have been presented, but as yet no agreement has been achieved; nor can any agreement be expected until morphological evidence—supported by experimental investigations—has shed more light on the pathogenesis of the condition.

As early as 1949, Wanke pointed out that in achalasia a regular pathologic finding is extensive replacement of the muscle layers by connective tissue in the region of the cardia as the final state after serous inflammation. Wanke gave these lesions the name of cardiac sclerosis. Such observations have also been made by Malm. Similar changes have been observed by Mosher and McGregor, and Stokes. Barrett, Beattie, Cameron, Correia Neto, Cross, Etzel, Hurst, Kay, Kelly, Lanzara, Lendrum, Mosher and McGregor, Rake, Rieder, and Stokes have described morphological changes in Auerbach's plexus. Judging by these investigations, it may be regarded as established that in achalasia the cardiac canal, usually 1 to 1.5 cm. long, is the site of organic changes with partial or complete destruction of the ganglion cells in Auerbach's plexus and more or less pronounced edema-sclerosis of the musculature. The following points, however, still require elucidation.

1. Are the morbid changes in Auerbach's plexus congenital (malformations with a varying loss of ganglion cells or alterations in their character), or are they acquired?

2. If the disease is acquired, the question arises whether the primary factor is involvement of the plexus with secondary organic sclerosis or whether serous inflammation of the esophageal wall is the primary lesion, which then involves the plexus with degenerative changes there as a consequence.

Kuntz and Lendrum assumed a congenital agenesia of the ganglion cells. The fact that the disease often begins to produce symptoms fairly early in life (average age at our clinic: 27 years) and that the condition is not rare even in childhood, and has even been diagnosed in infancy (Lortat-Jacob, Krasnova and Levin, Flynn, Kuypers, Cameron, Weber, Etzel and others) argue for this assumption. It is difficult to obtain confirmatory evidence because cases of early achalasia are seldom seen in the operating theater or in the dissecting room. Nevertheless, various observations argue for the disease being acquired. The findings made in Hirschsprung's disease are often compared with those seen in achalasia. In both, the cause is malformation in the region of the intramural plexus. In Hirschsprung's disease, it is a congenital agenesia limited to a narrow segment of the intestine. The symptoms appear in early infancy, in contradistinction to what is seen in achalasia, which rarely produces symptoms in the early stage of the disease. Therefore, the relatively few reports on cases of achalasia of recent development are all the more important. A fairly thorough search of the literature failed to reveal more than 1 described by Cross, 2 by Etzel, and 1 by Cameron.

In the case described by Cross, the patient was a man, aged 74, with a history of 18 months. Autopsy revealed intermingled degenerated and normal ganglion cells in the region of the cardia. Unlike the late cases, in the rest

of the esophagus the ganglia were of normal appearance and neither the esophageal wall nor the wall of the cardia showed any evidence of a pathologic condition. As pointed out by Etzel, it appears that the disease originates in the ganglion cells in Auerbach's plexus and that the other lesions seen in late cases are secondary.

In his cases of early achalasia, Etzel found that the inflammatory changes were strictly limited to the plexus. The morbid alterations were the same as those reported by Cross.

Cameron found similar lesions at autopsy of a child with achalasia. In his case, the inflammatory changes were limited essentially to the region of the plexus, the annular musculature was hypertrophic and some muscle fibers were fibrotic, while others showed hyaline and fatty degeneration.

According to Cannon, the parasympathetic ganglia of the esophagus are fairly resistant to various injurious agents. Even anoxia for 7 hours has no appreciable effect on their function. The ganglion cells of the sympathetic system on the other hand are said to be much more sensitive. Alvarez was unable to destroy the sympathetic ganglion cells by poisons. Even in the presence of chronic inflammatory processes in the environment, as in severe ulcerative colitis of 2½ to 30 years' duration, in which all of the layers of the wall were involved by inflammation, the ganglion cells were still intact.

Judging by the results of the investigations referred to above, it sounds less likely that the ganglion cells of the cardia can be injured by neighboring processes. Thus, the injurious factor must attack the ganglion cells directly if it is to produce a degenerative neuropathy of Auerbach's plexus. This can, according to Etzel, be brought about by deficiency of vitamin B, and, according to Cameron, by bacterial toxin. Cross was unable to trace a cause in his case.

The above-mentioned cases of early achalasia thus suggest, (1) the existence of an acquired form of achalasia and (2) that the disease originates in the ganglion cells and finally shows the picture of cardiac sclerosis described by Wanke, with disappearance of the ganglion cells. However, as reported by Wangensteen and Cross, apart from the unique finding of Etzel in a pigeon, it has as yet not been possible systematically to produce the picture of achalasia with degeneration of the ganglion cells in experimental animals. Cross expressed the view that a more concise concept of the sequence of events in the development of achalasia requires systematic production of the clinical syndrome in experimental animals. According to Merkel (1955), it has as yet not been possible to produce anything like true, permanent experimental achalasia.

In an endeavor to elucidate the pathogenesis we tried to produce achalasia in animals. We utilized knowledge of the fact that the tissue can be injured by cold and that, according to Tittel and Schneider, the effect of the cold on the tissue produces vasoconstriction, the intensity and duration of which varies with the amount of histamine liberated in the region studied and that this, in turn, depends on the intensity of the cold. Dontenwill confirmed Zetler's assumption of the causal importance of the histamine in injury by

cold; he observed that administration of antihistamine decreased both the intensity and the duration of the vasoconstriction. Judging by this investigation, it must be assumed that the decrease in the circulation persisting for some time after the application of the cold must enhance the immediate effect of the actual injury. According to Bötteher, nervous tissue is still more vulnerable to cold than the musculature and, apart from bone marrow, it is the tissue most sensitive to cold. Injury producing severe damage to the muscle tissue is thus also capable of injuring nervous tissue. It appears probable that the vasoconstriction produced by histamine will involve not only the vessels in the actual region exposed to the cold but also in the surroundings. In such an anoxemic region the protracted lack of oxygen supply may injure the nervous tissue there more than the somewhat less sensitive muscle tissue.

In an attempt to injure Auerbach's plexus, the cardia was exposed to local cold. The experiments were carried out on rabbits and dogs.

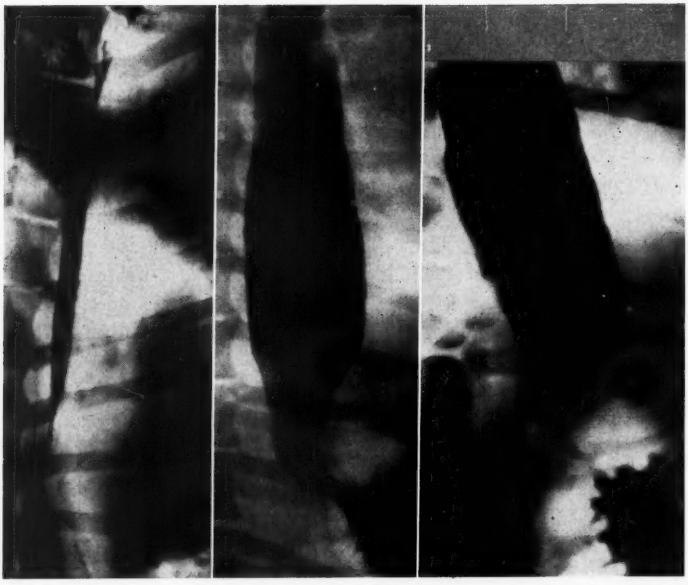
EXPERIMENTAL DATA

Carbon dioxide snow was applied locally to the region of the cardia via a specially constructed copper tube arrangement, a modification of the apparatus described by Speransky. In this way about 1 cm. of the cardiac region was exposed to a temperature of about –80° for half a minute.

The animals were anesthetized with morphine-atropine + Somnifen intravenously. Via an upper median incision, the stomach was exteriorized and the cardia made accessible. The surroundings of the cardia were draped and the copper tube placed around the esophagus and connected to a carbon dioxide cylinder for half a minute. The frozen region first turned white, but after a few minutes it became pink. The drapes were then removed and the abdomen was closed. Twenty-four hours later, when the effect of the anesthetic had worn off, the animals ran about in their cages as usual, and 2 days later they were eating as usual. The immediate postoperative course was never complicated.

During the subsequent 7 to 9 months the animals also appeared to feel well. In one group of 12 dogs, 4 showed a distinct, 3 a slight loss in weight; 4 had the same weight; and 1 had gained a little in weight. Swallowing difficulties, although relatively slight, occurred during the last months only in 2 animals; in three others there was occasional vomiting of undigested food during the experimental term. Some of the rabbits lost considerable weight toward the end of the experimental period. Most of them had, however, been killed earlier (one group per month) in order to study the progress of the changes in the region of the cardia.

Roentgen Findings.—The esophageal lumen in dogs, which is usually about the thickness of an ordinary lead pencil (Fig. 1, *A*), and through which food usually passes rapidly, was regularly dilated half a year after local freezing of the cardia, sometimes the dilatation was marked (megaesophagus), the wall was atonic and the passage of the food delayed. No organic stenosis was seen in the region of the cardia (Fig. 1, *B* and *C*).



A. *B.* *C.*

Fig. 1.—*A*, Normal esophagus (dog). *B*, Megaesophagus 7 months after cold injury (Dog 6). *C*, Megaesophagus 9 months after cold injury (Dog 1).

Fig. 2.—Pronounced muscle hypertrophy (compensation stage) in Dog 4.

Post-Mortem Examination.—Seven to 9 months after the experiment the animals were killed and the esophagus and stomach immediately removed and fixed in formalin.

Fig. 3.

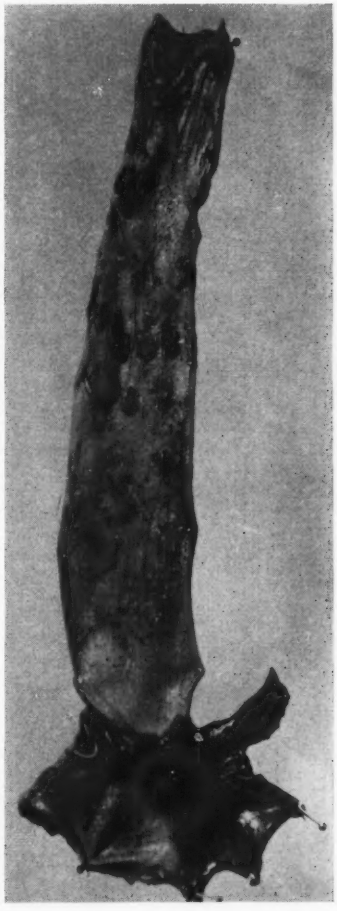


Fig. 4.

Fig. 3.—Distinct esophageal dilatation (commencing decompensation) in Dog 3.

Fig. 4.—Rabbit esophagus 12 weeks after cold injury. Note pronounced dilatation of esophagus and inflammatory changes of the mucosa because of commencing stercoral esophagitis with numerous superficial erosions and ulceration. The widening of the actual cardia is almost negligible.

The longitudinal cut surface of the esophagus showed pronounced muscular hypertrophy, especially in the lower third (Fig. 2). In such preparations, the dilatation was also more distinct than in unslit specimens (Figs. 3 and 4).

As a rule, the caliber of the esophagus had increased two- to threefold, but the cardia never showed any cicatricial stenosis after the injury by the cold.

Fig. 5.

Fig. 6.

Fig. 5.—Necrosis of the musculature of the cardia of a rabbit 48 hours after exposure to extreme cold. The muscle fibers are broken up (coagulation necrosis). Edema between the muscle fibers with swollen fibrocytes and invading histiocytes. (Hematoxylin and eosin; ×160; reduced ¼.)

Fig. 6.—Result of cold injury. Waxy (Zenker's) degeneration of the muscle fibers, loss of parenchyma and dissociation. (Hematoxylin and eosin; ×120; reduced ¼.)

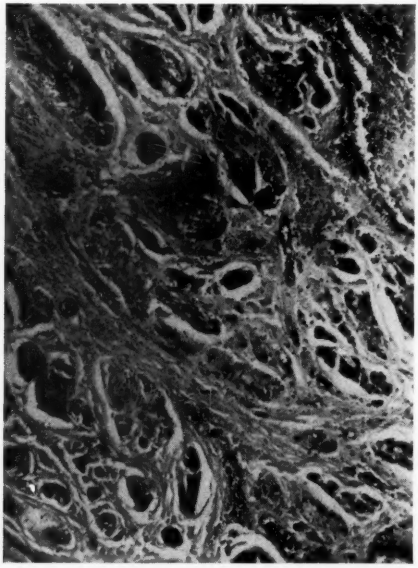


Fig. 7.—Tissue excised from human cardia with achalasia for comparison with Fig. 6. Severe loss of musculature with pronounced collagenous connective tissue between the dissociated and degenerated muscle fibers. Diffuse and focal round cell infiltration.

The cardia was closed in the usual way after death, and the mucosa was intact. The dilatation above the cardia was thus not due to organic stenosis but to a functional disturbance, i.e., the failure of the cardia to relax.

Histologic Findings.—In all of the animals, the cardia showed typical changes due to local freezing. The changes were more pronounced in the rabbits than in the dogs (Fig. 5).

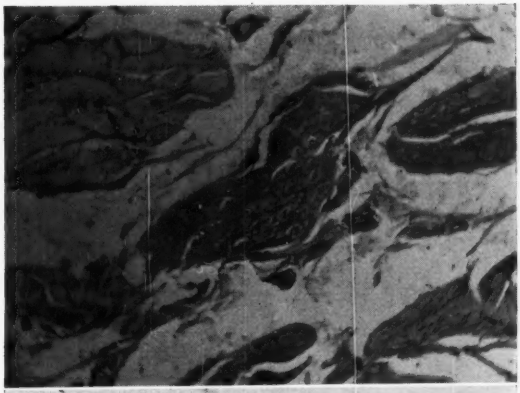


Fig. 8.

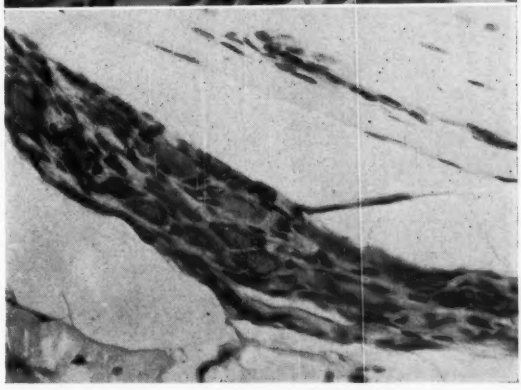


Fig. 9.

Fig. 8.—Ganglion of Auerbach's plexus of the cardia. Marked increase in supporting cells and connective tissue. The number of ganglion cells is decreased, although the total plexus is larger than normal. (Nissl's method; ×120; reduced ¼.)

Fig. 9.—Autonomic parasympathetic ganglion of the cardia with numerous degenerated ganglion cells. Vacuolation of the plasma, missing nuclei (confirmed in serial section). Increased number of capsule and supporting cells. (Nissl's method; ×200; reduced ¼.)

Fig. 6 shows a typical picture 9 months after injury by cold. The injury is limited to a region about 1 cm. wide (width of the copper tube conducting the carbon dioxide snow) and showed the same histologic picture as that seen in excised tissue from the cardia of human beings with achalasia (Fig. 7), namely, cardiac sclerosis.

The tissue above the frozen region showed marked hypertrophy of the musculature, but the mural layers were otherwise of normal appearance. On

Fig. 10.

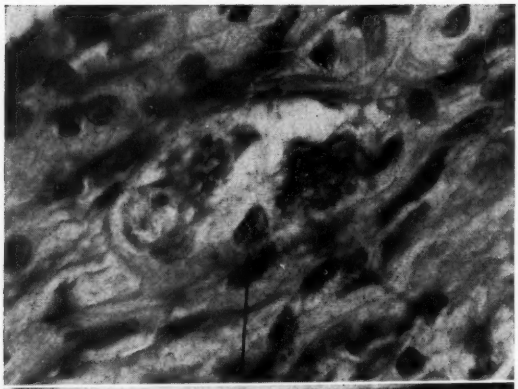


Fig. 11.

Fig. 12.

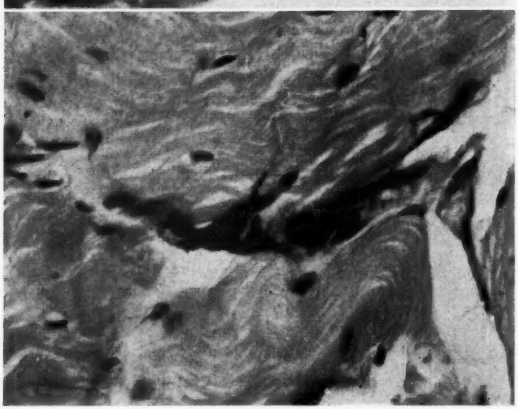


Fig. 10.—Initial change of a ganglion cell of Auerbach's plexus. Shrinkage of the cell, intracellular vacuolation, clumping of the tigroid, and the marginal position of the nucleus indicate degeneration. Arrow indicates a phagocytosing capsule cell. (Nissl's method; ×600; reduced ¼.)

Fig. 11.—Advanced changes of a ganglion cell of Auerbach's plexus. Pronounced shrinkage of the cell with retraction from the capsule and numerous small and large vacuoles in the cytoplasm. Complete destruction of the nucleus. Neuronophagia.

Fig. 12.—Growth of intercalary cells in the musculature of the esophagus 9 months after cold injury.

the other hand, between the annular and longitudinal musculature in the region of Auerbach's plexus there was a striking accumulation of round cells distinctly demarcating this otherwise hardly discernible region (Figs. 8 and 9).

Under high magnification it was seen that some of the ganglion cells had been completely or partly replaced by proliferating capsule and interstitial cells and some showed considerable degenerative changes (Fig. 10). Here various degrees of degeneration of the ganglion cells were observed with commencing neuronophagia. The ganglion cells were swollen, the Nissl bodies were clumped or dissolved, the ganglion cell nucleus was seen near the margin of the cell and in the periphery of the cell phagocyting supporting cell elements (Fig. 11).

The above-mentioned ganglion cell changes corresponded to those described by Etzel in 2 cases of early achalasia and the entire picture of the changes in Auerbach's plexus and in the surroundings was the same as that reported in the 4 early cases.

In our animal experiments, the cases may be regarded as early because all the animals were studied within 9 months of the freezing of the cardia with release of histamine and consequent lack of oxygen supply to Auerbach's plexus. But, even after such a short period, the further course of the injury was readily recognized (Fig. 12). The intercalary cells in the cardiac muscle coats were hyperplastic. According to Feyrter, such hyperplasia is a typical expression of the response of the vegetative nervous system to chronic irritation with an accumulation of sustentacular cells in the wall.

Further progress of the changes described above will, of course, lead to a final stage which Wanke found in a clinical series of achalasia and which he called sclerosis cardiae.

DISCUSSION

The observations made in the present investigation thus showed that by freezing the cardia in the rabbit and the dog it is possible to produce the clinical picture of achalasia with muscular hypertrophy of the esophageal wall and secondary dilatation of the esophagus oral to the cardia. Roentgenography never showed cicatricial stenosis, and the mucosa was always intact. Histologically the frozen region resembled the end stage of achalasia described by Wanke as cardiac sclerosis (Figs. 13 and 14). Oral to the frozen region, Auerbach's plexus showed striking changes and corresponded in all respects to that described by Cameron, Cross, and Etzel in cases of early achalasia. From this region the disease proceeded via the intercalary cells in the musculature of the cardia and finally resulted in complete structural degeneration—cardiac sclerosis.

According to the present experiments, the first stage in the development of achalasia is an impairment of the circulation with consequent destruction of the neural elements of the cardia. This circulatory disturbance is due to the fact that the histamine released in the cardia region exposed to the cold results in protracted vasoconstriction not only of the actually chilled region

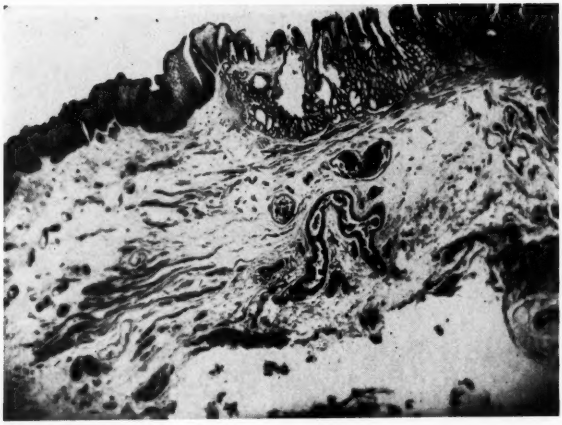


Fig. 13.—Pronounced cardiac sclerosis of a dog 9 months after cold injury. The normal wall layers have been substituted by fibrous connective tissue; only small rests of the musculature are visible.

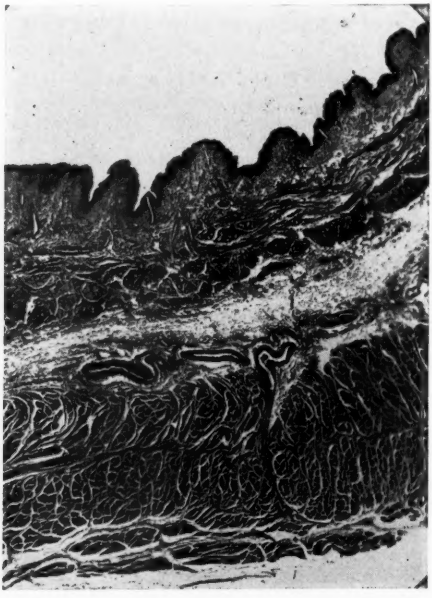


Fig. 14.—Normal wall layers of the esophagus (dog) as a comparison with Fig. 13.

but also of the surroundings. This vasocontriction is followed by a period of spontaneous contractions (Zetler, Dontenwill). Owing to their relatively large requirement of oxygen, the ganglion cells are extremely sensitive to hypoxia and readily succumb. Clinically this produces the picture of achalasia.

Similar changes of the neural elements of the brain owing to hypoxia are known, e.g., following electro-shock treatment and following the administration of Cardiazol and vasopressin.

SUMMARY

A clear conception of the normal anatomy and physiology of the region of the cardia is necessary for understanding the pathophysiology of achalasia.

A review of the literature and personal experimental investigations suggested the following conclusions.

1. In the region of the cardia there appears to be no anatomic sphincter analogous to the pylorus, the vesical sphincter, or the anal sphincter. The closure of the esophagus is brought about by a number of factors, including the angle at which the esophagus enters the stomach with the formation of the plica cardiaca, and the natural tone of the cardia.

2. The opening of the cardia at the end of deglutition is brought about by vagal fibers extending from the nucleus pigmentosus and innervating the striated musculature of the upper third of the esophagus. They are not true parasympathetic fibers but, analogous to the motor fibers of the vagus innervating the larynx, occupy a special position in this nerve. Their antagonist is not the sympathetic system but the neuromuscular system of the cardia itself which possesses considerable tone even in the resting state. On irritation of the sympathetic system the tone of the cardia is increased but immediately decreases on termination of the irritation. Even after operation with removal of all the sympathetic fibers, cardiac function is still normal.

The experiments showed that it is possible to produce experimental achalasia simulating that seen in human beings. On the basis of these experiments and studies of human cases of achalasia of recent origin and therefore early in development, it was possible to form a fairly clear opinion of the pathogenesis of the disease.

1. Achalasia appears to originate in Auerbach's plexus with typical degeneration of the ganglia, agreeing entirely with the findings seen in early cases of human achalasia. With this as a point of departure the mural layers of the cardia degenerate probably gradually, until they reach the final stage of degeneration described by Wanke as cardiac sclerosis.

2. Judging by the human cases of early achalasia on record, there appears to exist an acquired form of achalasia.

3. In the experiments described, the causal factor was chronic anoxemia with destruction of Auerbach's plexus as a consequence.

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THE GASTROESOPHAGEAL SPHINCTER MECHANISM

II. Further Experimental Studies in the Dog

Johan H. Meiss, M.D., John H. Grindlay, M.D.,** and F. Henry Ellis, Jr., M.D.,*** Rochester, Minn.*

OPINION varies as to the nature of the mechanism which normally prevents the reflux of gastric contents into the esophagus. Among the various hypotheses which have been advanced, the following seem most worthy of investigation: (1) an intrinsic gastroesophageal sphincter, (2) the acute esophagogastric angle, (3) the diaphragmatic "pinchcock," and (4) a mucosal valve or rosette.

Recent studies[4] from this laboratory showed that the diaphragm is not the major factor responsible for gastroesophageal continence, and further suggested that a sphincteric mechanism of undefined nature resides in the region of the esophagogastric junction. These studies did not indicate whether an intrinsic sphincter exists or whether the oblique entry of the esophagus into the stomach, associated perhaps with a valve flap of mucous membrane, is responsible.

It is the purpose of this paper to report further investigation concerning the nature of the mechanism responsible for gastroesophageal continence. In these studies, carried out on dogs, the various mechanisms mentioned were eliminated one by one in an attempt to define more exactly the mechanism of chief importance in prevention of reflux.

METHOD

Adult mongrel dogs were anesthetized with intravenously administered pentobarbital sodium (Nembutal); and in operations in which the thorax was opened, an intratracheal positive pressure apparatus was put in place.

Group I.—In animals of Group I the esophagogastric junction was removed and the esophagogastric anastomosis was made in different ways. In every dog the distal 2 cm. of esophagus and the proximal 2 cm. of stomach were removed. The anastomosis was made in two layers, with a continuous catgut suture for the mucosal layer and interrupted cotton sutures for the muscular layer.

From the Mayo Clinic and Foundation, Rochester, Minn. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.
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*Fellow in Surgical Research, Mayo Foundation.
**Section of Surgical Research, Mayo Clinic and Mayo Foundation.
***Section of Surgery, Mayo Clinic and Mayo Foundation.

Group II.—The acute esophagogastric angle was eliminated in animals of Group II by resection of the fundus or by division of the stomach 2 cm. below the esophagogastric junction and anastomosis of the upper rim of the stomach to the top of the fundus.

Group III.—Animals in Group III underwent formation of a partial thoracic stomach. The phrenoesophageal ligaments were incised and the diaphragm was attached to the stomach at a lower level, so as to eliminate the diaphragmatic pinchcock mechanism.

Group IV.—The mucosal rosette was eliminated in animals of Group IV, in addition to elimination of the acute esophagogastric angle, and the diaphragmatic pinchcock. The stomach was divided 2 cm. below the esophagogastric junction and the proximal rim of the stomach was anastomosed to the fundus. In addition, the mucosa in both this small rim of stomach and the lower 1 cm. of esophagus was removed and replaced by mucosa from the fundus.

All dogs received penicillin and streptomycin intramuscularly after operation. The dogs were given a liquid diet for a week and were fed a meat meal twice a day after that. No other method to increase the output of hydrochloric acid was used because frequent feeding was considered more nearly physiologic than the injection of histamine.

In all dogs, except those undergoing esophagogastrectomy, the vagus nerves were preserved. One dog in Group I and 5 dogs in Group III died after the operation as a result of cutting through of the sutures between the stomach and the diaphragm. In these dogs the stomach was found, dilated, in the thorax. These dogs have not been included in the tables. The dog in Group I died on the eighth day after the operation and did not show any esophagitis. Esophagitis similarly did not develop in dogs in Group III.

TABLE I. RESECTION OF THE ESOPHAGOGASTRIC JUNCTION*

ADDITIONAL PROCEDURE	DOG	INITIAL ESOPHAGITIS, AFTER DAYS	KILLED OR DIED, AFTER DAYS	FINDINGS AT NECROPSY
I,A Anastomosis below the diaphragm	1	52 first examination	Killed 85	Linear esophagitis
	2	130 second examination	Killed 150	Linear esophagitis
	3	36 first examination	Killed 51	Linear esophagitis
I,B Anastomosis above diaphragm	4	45 first examination	Killed 78	Ulceration
	5	48 first examination	Killed 148	Linear esophagitis
	6	42 first examination	Killed 70	Ulceration
	7	--------	Died 25	Perforated ulcer
	8	--------	Died 15	Perforated ulcer
	9	--------	Died 29	Ulceration
I,C Creation of acute esophagogastric angle, anastomosis above diaphragm	10	--------	Died 16	Ulceration
	11	--------	Died 9	Ulceration
	12	--------	Died 7	Perforated ulcer
	13	--------	Died 7	Perforated ulcer
	14	--------	Died 25	Linear esophagitis
	15	--------	Killed 27	Ulceration
I,D Narrowing distal esophagus, anastomosis below diaphragm	16	57 first examination	Killed 76	Ulceration
	17	--------	Died 38	Ulceration
	18	105 second examination	Killed 105	Linear esophagitis

*See also Fig. 1.

RESULTS

Group I. Removal of the Esophagogastric Junction.—

Although it has been frequently found that resection of the esophagogastric junction is followed by esophagitis, it was thought wise to perform this procedure in a number of dogs in order to learn if it was possible to prevent esophagitis by leaving the anastomosis below the diaphragm (Fig. 1 [I,A and D]), by

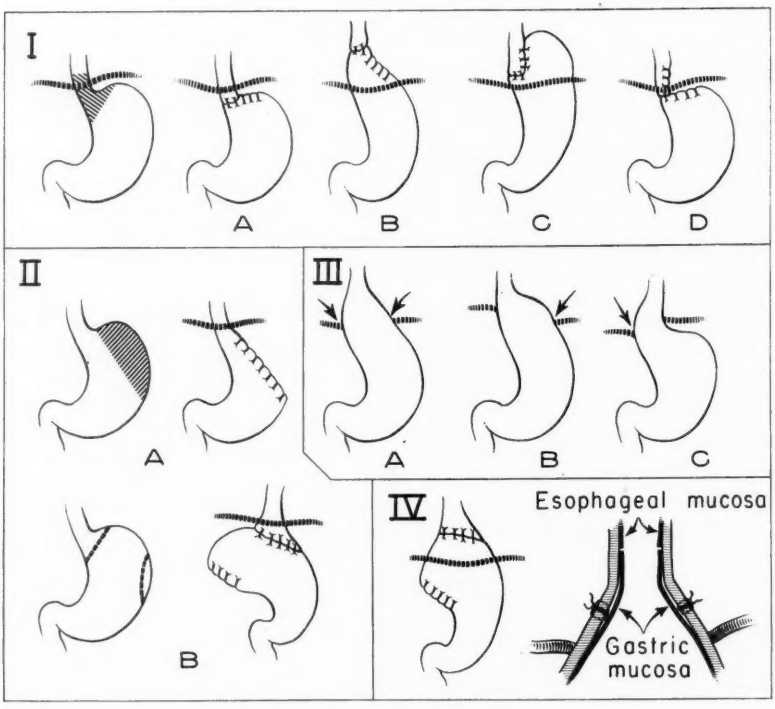

Fig. 1.—The experimental preparations used.

Group I. Resection of the esophagogastric junction with anastomosis below the diaphragm (*A* and *D*) above the diaphragm (*B*) with acute esophagogastric angle (*C*) and with narrowed distal esophagus (*D*).

Group II. Elimination of the acute angle. *A*, Resection of the fundus. *B*, Anastomosis of small upper rim of stomach to the fundus.

Group III. Elimination of the diaphragmatic pinchcock by division of both sides (*A*) or either side (*B* and *C*) of the phrenoesophageal ligament and reattachment of the diaphragm to the stomach at a lower level.

Group IV. Anastomosis of small upper rim of the stomach to the fundus, replacement of the mucosa in the upper rim of stomach and lower 1 cm. of esophagus by fundic mucosa. Anastomosis left in the thorax.

forming a new sharp esophagogastric angle (Fig. 1 [I,C]), or by narrowing the distal part of the esophagus to half its circumference (Fig. 1 [I,D]). In 6 dogs the anastomosis was left above the diaphragm (Fig. 1 [I,B]). An acute angle was produced by suturing the fundus to the esophagus and in some

animals by fixing the angle by means of a band of fascia, attached to the diaphragm. The distal part of the esophagus was narrowed by excision of a triangular portion of the esophageal wall.

Esophagitis developed in all animals in this group (Fig. 2). It appears that the most severe degree of esophagitis developed in the shortest time in the dogs in which a new angle was made and in which the greatest part of the stomach was above the diaphragm (Table I).

Conclusion: An acute esophagogastric angle and the diaphragmatic pinchcock cannot prevent esophagitis after removal of the esophagogastric junction in dogs.

Fig. 2.—Specimen of stomach and esophagus of Dog No. 14 in Group I,C. The esophagus shows marked esophagitis with ulceration.

Group II. Elimination of the Acute Esophagogastric Angle.—

The esophagogastric angle was made obtuse in two ways to evaluate the importance of a sharp esophagogastric angle in the prevention of reflux. In some dogs the fundus was removed (Fig. 1 [II,A]). In the other dogs the stomach was transected 2 cm. below the gastroesophageal junction, and subsequently the proximal portion was anastomosed to the fundus (Fig. 1 [II,B]). Esophagitis did not develop in any of the dogs submitted to this procedure (Table II; Figs. 3 and 4,*a*).

TABLE II. ELIMINATION OF ACUTE ESOPHAGOGASTRIC ANGLES*

PROCEDURE	DOG	INITIAL ESOPHAGITIS, AFTER DAYS	KILLED, AFTER DAYS	FINDINGS AT NECROPSY
II,A Resection of fundus of stomach	19	--------	250	No esophagitis
	20	--------	144	No esophagitis
	21	--------	78	No esophagitis
	22	--------	78	No esophagitis
II,B Anastomosis of small upper rim of stomach to the fundus	23	--------	229	No esophagitis
	24	--------	194	No esophagitis
	25	--------	188	No esophagitis
	26	--------	287	No esophagitis

*See also Fig. 1.

Conclusion: An acute esophagogastric angle is not necessary to prevent reflux esophagitis in dogs.

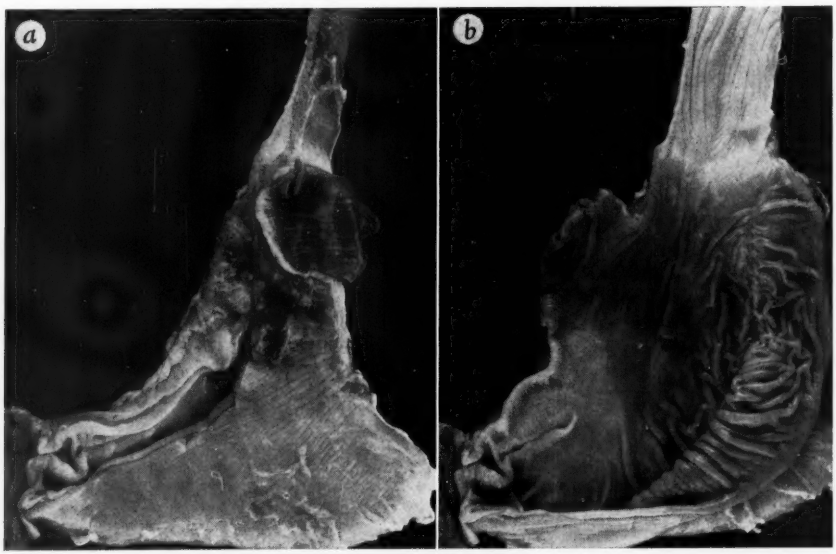

Fig. 3.—Specimen of stomach and esophagus of Dog No. 20 in Group II,A. No esophagitis was found after resection of the fundus of the stomach. *a*, Stomach incised but unopened. *b*, Stomach and esophagus opened.

Group III. Elimination of the Diaphragmatic Pinchcock.—

The diaphragmatic pinchcock was removed by division of both sides of the phrenoesophageal ligament in some dogs (Fig. 1 [III,A]), only the left in others (Fig. 1 [III,B]) and only the right side of this ligament in others (Fig. 1 [III,C]). In all, the stomach was placed in the thorax for a distance of about 3 or 4 cm. and the diaphragm was attached to it in the new position. Care was taken to leave a wide communication between the supradiaphragmatic and infradiaphragmatic portion of the stomach. The different procedures to

TABLE III. ELIMINATION OF DIAPHRAGMATIC PINCHCOCK*

PROCEDURE	DOG	INITIAL ESOPHAGITIS, AFTER DAYS	KILLED, AFTER DAYS	FINDINGS AT NECROPSY
III,A Both sides of phrenoesophageal ligament attached to stomach	27	--------	222	No esophagitis
	28	--------	83	No esophagitis
	29	--------	61	No esophagitis
	30	--------	59	No esophagitis
III,B Only left side of phrenoesophageal ligament attached to stomach	31	--------	117	No esophagitis
	32	--------	105	No esophagitis
	33	--------	103	No esophagitis
	34	--------	89	No esophagitis
	35	--------	74	No esophagitis
	36	--------	87	No esophagitis
III,C Only right side of phrenoesophageal ligament attached to stomach	37	--------	96	No esophagitis
	38	--------	96	No esophagitis

*See also Fig. 1.

Fig. 4.—*a*, Specimen of stomach and esophagus of Dog No. 25 in Group II, B. No esophagitis was found after transposition of a small upper rim of stomach to the fundus. *b*, Specimen of stomach and esophagus of Dog No. 30 of Group III, A. Formation of a partial thoracic stomach was not followed by esophagitis.

obviate the diaphragmatic pinchcock were done because Guiseffi and associates[10] in this laboratory found marked esophagitis when they removed the muscle of the left portion of the right crus of the diaphragm.

Esophagitis did not develop in the dogs in the present study (Table III; Fig. 4,*b*).

Conclusion: The diaphragmatic pinchcock is not an essential mechanism for the prevention of reflux esophagitis in dogs.

Group IV. Elimination of the Mucosal Rosette in Addition to the Acute Esophagogastric Angle and Diaphragmatic Pinchcock.—

The stomach was cut 2 cm. below the esophagogastric junction and the mucosa in the small rim of stomach was removed, together with the mucosa of the distal 1 cm. of esophagus. This gastric rim was anastomosed to the fundus

Fig. 5.—Specimen of stomach and esophagus of Dog No. 41 of Group IV. No esophagitis was found when a small upper rim of stomach was anastomosed to the fundus, the mucosa of the upper rim of stomach and 1 cm. of esophagus were replaced by fundic mucosa and the anastomosis was left in the thorax.

TABLE IV. ELIMINATION OF MUCOSAL VALVE OR ROSETTE IN ADDITION TO ACUTE ESOPHAGOGASTRIC ANGLE AND DIAPHRAGMATIC PINCHCOCK*

PROCEDURE	DOG	INITIAL ESOPHAGITIS, AFTER DAYS	KILLED, AFTER DAYS	FINDINGS AT NECROPSY
Anastomosis of small upper rim of stomach to fundus, replacing	39	--------	83	No esophagitis
mucosa by fundic	40	--------	78	No esophagitis
mucosa, anastomosis	41	--------	75	No esophagitis
above the diaphragm	42	--------	70	No esophagitis

*See also Fig. 1.

in such a way that mucosa from that part of the stomach replaced the mucosa previously removed. The anastomosis was left 4 cm. above the diaphragm (Fig. 1 [IV]). Esophagitis did not develop in these dogs (Table IV; Fig. 5).

Conclusion: The acute esophagogastric angle, the diaphragmatic pinchcock, and a specific mucosal valve or rosette are not essential to prevent esophagitis in dogs. An intrinsic sphincter mechanism in the region of the esophagogastric junction was the only possible mechanism which prevented esophagitis in this group.

COMMENT

The acute esophagogastric angle, maintained by the diaphragm, was thought to play an important role in the prevention of reflux by Marchand,[13] who demonstrated that the pressure necessary to force fluids from the esophagus into the stomach was much less than that necessary to force it in the opposite direction. The importance of the oblique entry of the esophagus into the stomach also was emphasized by Allison.[1] Savage[15] found esophagitis in dogs in which he had removed the fundus of the stomach. However, Hoag and associates[11] found that as long as a small rim of stomach was left distal to an intact esophagogastric junction, partial resection of the stomach was not followed by esophagitis, even though the acute gastroesophageal angle was eliminated. Our findings are in keeping with those of these latter workers. The acute esophagogastric angle does not appear necessary for the prevention of reflux in the dog.

The importance of the diaphragmatic pinchcock mechanism in the prevention of reflux has been stressed by Jackson[12] and Allison,[1] among others. Previous work from this laboratory by Braasch and one of us (Ellis)[4] discounted the importance of this mechanism, at least in dogs. They created an abdominal esophagus in dogs by elevating the hiatus to a point 2 to 3 cm. above the gastroesophageal junction. Esophagitis did not develop in the animals, which suggested that something other than the diaphragm protected the distal part of the esophagus against reflux in these dogs. Friesen and Miller[8] bypassed the esophagogastric junction in dogs, leaving the esophageal stump either above or below the diaphragm. In their dogs, esophagitis developed above the esophagogastric anastomosis, but the esophageal stump remained entirely free from disease. The same authors showed that formation of a partial thoracic stomach in dogs was followed by esophagitis only when the hiatus was made very narrow. When esophagitis occurred it was accompanied by gastritis in the supradiaphragmatic portion of the stomach. It would appear from their experiments that neither an acute esophagogastric angle nor the diaphragmatic pinchcock is necessary to prevent esophagitis in dogs. The results of our own experiments confirm these findings.

Guiseffi and associates,[10] however, did find esophagitis in dogs in which the phrenoesophageal ligament was not divided but in which the muscle bundle of the left side of the right diaphragmatic crus was removed. In our experiments, in which the phrenoesophageal ligament was cut and the diaphragm was attached to the stomach at a lower level, esophagitis did not develop. An attempt

was made to prevent obstruction of the supradiaphragmatic gastric pouch in our experiments, and this may account for the findings which differ from those of Guiseffi and associates.

Nauta[14] studied the movements of the esophagus by means of roentgen cinematography and by observing the cardia through a gastric fistula. He did not find any sphincterlike action in the distal part of the esophagus and concluded that the closure of the cardia is formed by a rosette of stomach mucosal folds, supported by a valvular mechanism as a result of the oblique entry of the esophagus into the stomach. On the other hand, Cohn and Magladry[6] removed the mucosa of 3 to 4 cm. of the distal part of the esophagus and covered the defect with gastric mucosa, brought up by submucous dissection. Esophagitis did not develop. These workers concluded that the mucosal rosette at the esophagogastric junction is not responsible for the prevention of reflux as long as the angle of entrance of the esophagus into the stomach is preserved.

The results of our experiments show that it is possible to remove the diaphragmatic pinchcock, to make the gastroesophageal angle obtuse and, in addition, to replace the mucosa at the gastroesophageal junction without the development of esophagitis. We therefore must conclude that an intrinsic mechanism, a sphincter, must be responsible for the remarkable fact that esophagitis was not found in any dog in our experiments unless the esophagogastric junction had been removed. Although most anatomists did not find a definite sphincter cardiae, Fyke and associates[9] and Atkinson and associates,[2] using the technique of intraluminal measurements of pressure, demonstrated the presence of a definite sphincteric mechanism at the esophagogastric junction in healthy persons. This mechanism recently has been demonstrated also in dogs.[16] Braasch and one of us (Ellis),[4] and Brackney and associates[5] showed that a long myotomy through the muscles of the esophagus and cardia may be followed by esophagitis in dogs. Presumably in these experiments the esophageal sphincter was completely divided.

Care should be exercised in applying the results of animal experiments to human beings. These experimental results, which emphasize an intrinsic sphincter mechanism as the important factor in the prevention of reflux, may seem at first glance to be at variance with clinical experience. The occurrence of esophagitis in patients with sliding esophageal hiatal hernia in whom, presumably, the intrinsic sphincter remains intact is well known. We share the opinion of Effler and Groves[7] on this problem, namely, that the diaphragm, placed in a position in which it can impair the passage of gastric contents between the supradiaphragmatic and infradiaphragmatic parts of the stomach, may lead to esophagitis in the presence of sliding hernia. Furthermore, Atkinson and his associates[3] have demonstrated, by studies of esophageal motility, a definite correlation between the height of the pressure barrier at the esophagogastric junction and the presence or absence of symptoms of reflux in patients with hiatus hernia. They concluded that the tone of the intrinsic sphincter is of cardinal importance in preventing reflux under these circumstances.

SUMMARY

Experiments were carried out in dogs to investigate the mechanism which prevents reflux esophagitis. It was found that resection of the esophagogastric junction was followed by esophagitis in every instance. Esophagitis was not prevented when the anastomosis was brought below the diaphragm, when the esophagus was narrowed, or when an acute angle was created between the esophagus and the stomach.

Esophagitis did not develop when the acute esophagogastric angle was eliminated, the diaphragmatic pincheock was removed and the mucosa at the esophagogastric junction was replaced by fundic mucosa. It was concluded that a physiologic, if not an anatomic, sphincter must reside in the region of the esophagogastric junction, independent of the diaphragm, the acuteness of the esophagogastric angle and a specific mucosal valve or rosette. The sphincter was found to be capable of preventing esophagitis in dogs under the conditions of these experiments.

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MULTIPLE PRIMARY CANCER OF THE LUNG

C. L. N. Robinson, F.R.C.S.(C), F.R.C.S., and C. A. Jackson, M.B.E., F.R.C.S., London, England*

THIS STUDY presents 9 cases of dual primary cancer of the lung seen in a series of 500 cases of bronchial carcinoma at one Thoracic Surgical Unit. Multiple primary tumors of the lung have not been widely recognized or reported in the literature, yet with the gradual acceptance of air pollution and smoking as causative factors in the etiology of this disease, it is not surprising that multiple sites of origin should occur. As pulmonary cancer is now the commonest male cancer, its appearance in two lungs or twice in one lung might be expected.

Billroth[1] first drew attention to multiple primary malignant neoplasms at several sites, but his criteria of multiple malignancy were stringent and could not be applied to multiple tumors in a single organ. To satisfy a diagnosis of multiple primary malignancy he postulated that (1) each tumor must have an independent histologic appearance, (2) each tumor must arise in different situations, and (3) each tumor must produce its own metastases. Another rule, that of Mercanton, can only be applied to necropsy material: if, after the removal of two or more tumors, no further metastases develop, each tumor may be considered primary.

The criteria for diagnosing multiple primary tumors in this series have been macroscopic and microscopic independence. It is easy to distinguish macroscopic independence, but the difficulty in accepting the duality of origin of primary pulmonary cancer on histologic grounds depends on whether pleomorphism can be excluded in serial sections of any one tumor.

Several writers have discussed pleomorphism in bronchial carcinoma: Willis,[2] reporting on 84 necropsy cases, found a combined histologic pattern in 23 per cent or, conversely, an homogeneous pattern in 77 per cent; in 53 per cent of the cases of McGrath and others,[3] the tumor contained from 2 to 5 different histologic patterns, arranged in such a manner as to suggest initial independence and ultimate fusion—he concluded that neoplasms arose from more than one site and clinical recognition did not occur till coalescence of independent growths had been completed.

From the Thoracic Surgical Unit, St. Charles' Hospital, Ladbroke Grove, London.W.10, England.

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*Present address: Harefield Hospital, Harefield, Middlesex, England.

More recently, however, Walter and Pryce[4, 5] have cleared the problem of pleomorphism in bronchial carcinoma—while some cases presented a complex histologic picture, by adhering to established criteria and examining numerous blocks from large tumors, they were able to classify all growths in their series into 5 types: oat cell, squamous cell, adenocarcinoma, polygonal cell carcinoma and a single rare type of metastasizing adenoma. Secondary changes such as squamous metaplasia, clear cell formation, and giant cell formation could be recognized as such in individual tumors, but did not obviate a classification into a single cell type.

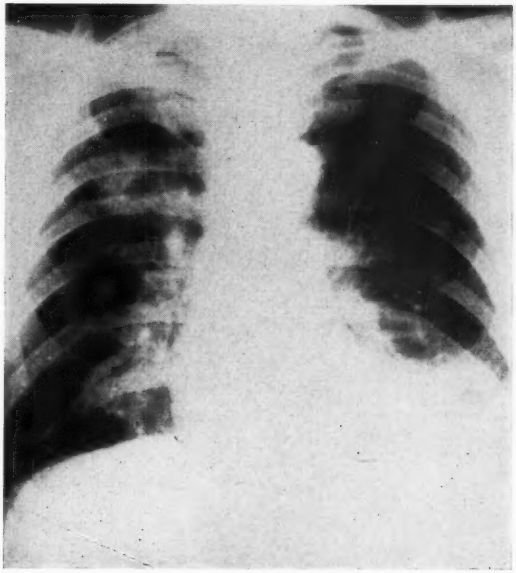

Fig. 1.—Case 2. Roentgenogram showing cavitated lesion in the right upper lobe due to oat cell carcinoma and segmental shadow in the left posterior basal segment due to squamous cell carcinoma.

The histologic specimens in this series have been studied by three independent pathologists and have been considered to be sufficiently diverse as to represent dual primary cancer. The two primary cancers presented simultaneously in 8 patients, and in 1 the second developed 5 years after a presumed cure of a contralateral primary tumor by lobectomy. In 4 cases, the tumors were on the same side, and in 5 cases in opposite lungs. All the patients were males.

CASE REPORTS

CASE 1.—A. H., aged 51, complained of recurrent staining of sputum and left chest pain. The admission radiograph showed partial deflation of the left lower lobe. Bronchoscopy showed an abnormal appearance in both lower lobe bronchi, consisting of edematous mucosa and nodular granulations. The biopsy fragment from the right side showed squamous

metaplasia, suggestive of neoplasm, and the left was normal. With treatment, the left side cleared but the right lower lobe showed partial deflation. A second bronchoscopy showed appearances similar to the previous one, with less inflammation. The biopsy from the left contained areas of oat cell carcinoma, and from the right, areas of inflammation and small fragments of growth. After consultation with several pathologists, it was agreed that a

Fig. 2.

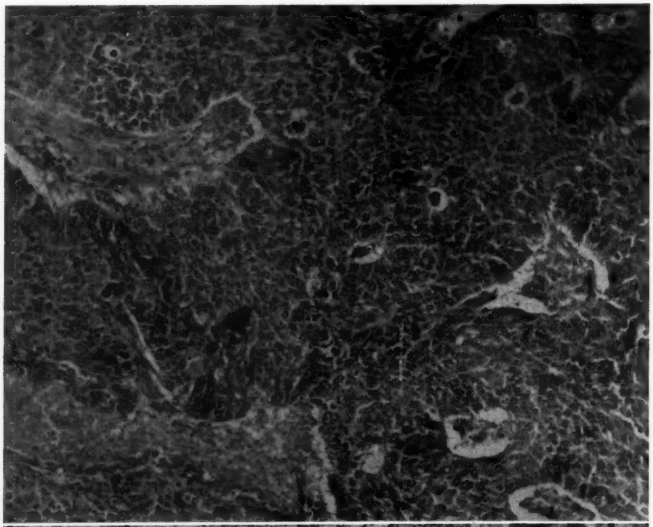

Fig. 3.

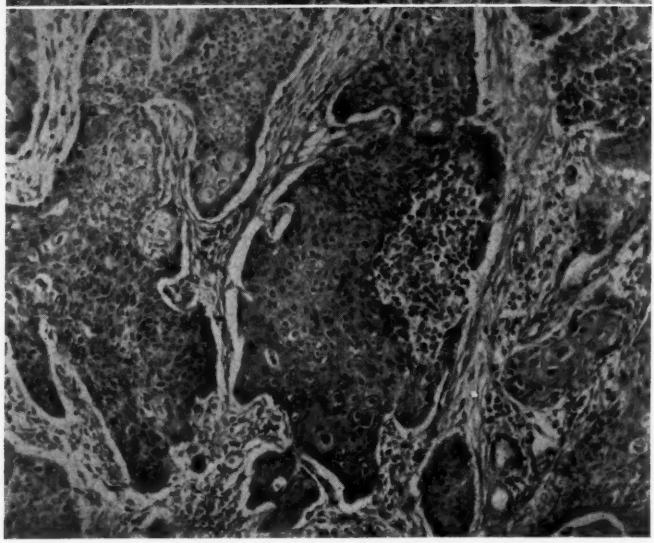

Fig. 2.—Case 3. Photomicrograph of left upper lobe tumor shows large oat cells. (×103.)
Fig. 3.—Case 3. Photomicrograph of squamous cell tumor of left lower lobe. (×103.)

diagnosis of bilateral carcinoma was unlikely, and that the probable diagnosis was squamous metaplasia, associated with chronic inflammation. This patient was returned to the care of his physician, and died one year later. Necropsy revealed a large oat cell carcinoma of the left lower lobe while on the right side a small nodular squamous cell tumor partially obstructed the bronchus.

CASE 2.—W. C., aged 55, complained of cough and green sputum, hemoptysis on one occasion, and loss of weight. A radiograph (Fig. 1) showed a cavity in the right upper lobe and deflation of the posterior basal segment of the left lower lobe. Initially he had been treated with antituberculous drugs. After a month he had a massive hemoptysis requiring transfusion, and there was no radiological improvement—he was then treated as for an abscess of the right upper lobe with spill over into the left lower lobe. Bronchoscopy

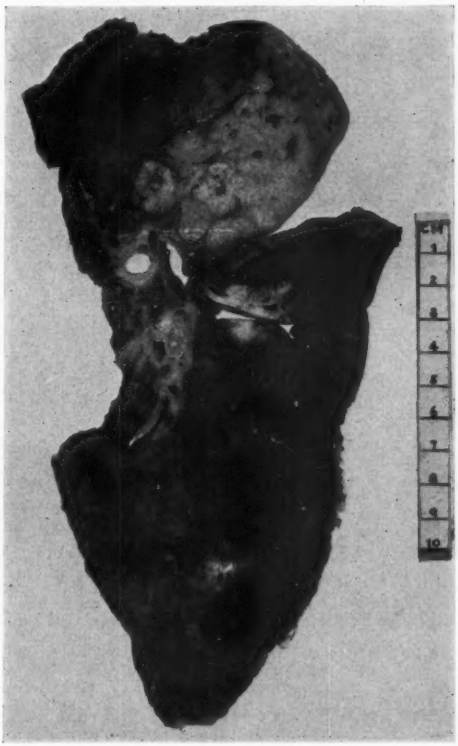

Fig. 4.—Case 4. Half-lung section shows large tumor of left upper lobe (oat cell type) and smaller tumor in left lower lobe (squamous cell type).

a month later showed slight narrowing of the left lower lobe bronchus, the mucosa of which bled easily. Blind biopsies were taken from the posterior basal segment and from a bleeding right upper lobe. The histologic appearance of the tissue from the left lower lobe was that of squamous cell carcinoma, and from the right upper lobe, oat cell carcinoma.

He had a course of deep x-ray therapy but he died a year later.

CASE 3.—B. C., aged 57, was admitted with a history of blood-stained sputum once and a cough for a month. A radiograph showed peripheral shadows in the left upper lobe and

left lower lobe. Bronchoscopy showed concentric narrowing of the left lower lobe bronchus, but the biopsy was negative. A left pneumonectomy was performed. Histologic studies revealed an oat cell carcinoma of the left upper lobe (Fig. 2) and a keratinizing squamous carcinoma of the left lower lobe (Fig. 3) with extensive involvement of lymph nodes.

This man died 2 years later of a recurrence.

CASE 4.—H. B., aged 55, complained of a dry cough for 6 months. A radiograph showed a large ill-defined opacity in the left upper lobe. Bronchoscopy was normal. A bronchogram showed an irregular rattail obstruction of the apicoposterior segment of the left upper lobe and a filling defect of the upper branch of the apical segment of the left lower lobe. A left pneumonectomy was performed. There was a large tumor in the upper lobe and a smaller tumor in the lower lobe (Fig. 4). Histologic study revealed the former to be of an oat cell type, and the latter to be squamous cell in type. He made a satisfactory early recovery, but died 2 months later of liver metastases.

Fig. 5.—Case 7. Chest radiograph shows bilateral hilar shadows with a more peripheral shadow in the right upper lobe.

CASE 5.—A. K., aged 62, complained of dyspnea on exertion and tightness across the chest. A radiograph showed two peripheral shadows, seen best in the lateral film, one in the lingula and the other in the posterior basal segment of the lower lobe. Bronchoscopy was negative. A left pneumonectomy was performed easily. The lingular tumor was squamous in type, and the other oat cell in type. The patient is well and working.

CASE 6.—W. S., aged 46, was admitted with a small peripheral shadow in the right lower lobe for which a lower lobectomy was performed. The histologic appearance was that of a polygonal cell carcinoma. He remained in good health for over 5 years, when he developed sudden precordial pain and shock. A radiograph showed a segmental lesion in the left upper lobe. He died primarily from cardiac infarction, but a necropsy showed a pleomorphic carcinoma of the left upper lobe which was basically adenocarcinoma, with extensive invasion of lymph nodes, and metastases in the brain and kidneys.

CASE 7.—L. W., aged 64, complained of dyspnea on exertion and chest tightness. A radiograph showed hilar shadows in both upper lobes (Fig. 5). He collapsed and died suddenly before investigations were completed. Necropsy revealed a recent cardiac infarction, an oat cell carcinoma of the right upper lobe bronchus and a peripheral necrotic squamous carcinoma in the left upper lobe with extensive liver metastases.

CASE 8.—H. D., aged 62, complained of loss of weight and left inframammary pain on exertion. A radiograph showed shadows in the left upper lobe and the left lower lobe (Fig. 6). Bronchoscopy revealed growth protruding from the apicoposterior segment of the left upper lobe and narrowing of the left lower lobe bronchus. A palliative pneumonectomy was accomplished with difficulty. The upper lobe lesion was an oat cell tumor and the lower lobe contained an adenocarcinoma. He is at present well and working, 6 months after operation.

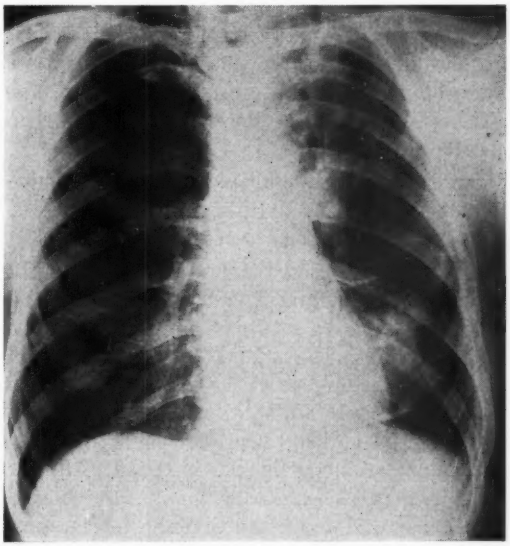

Fig. 6.—Case 8. Chest radiograph shows a peripheral lesion in the left lower lobe due to adenocarcinoma and a central lesion in the left upper lobe with distal infiltration due to an oat cell tumor.

CASE 9.—A. J. R., aged 80, was admitted in extremis and died the same day. A necropsy showed emphysema and bronchitis, with an oat cell carcinoma of the posterior basal segment of the right lower lobe, and a squamous carcinoma of the apical segment of the left upper lobe.

DISCUSSION

Dual carcinomata in other single organs (breast, colon, testis) have been occasionally reported. The incidence of multiple malignancy affecting all sites was estimated by Warren and Gates[6] as 1.84 per cent. This percentage resulted from analyzing several reported series, including surgical and necropsy material, and finding 546 satisfactory cases in 29,740 studied. When smaller series were examined (less than 500 cases) the incidence varied between 0.5 per cent and 4.3 per cent. Our 9 cases occurred in a series of 500 proved

neoplasms of the lung, and the number is too small to be significant statistically. They concluded that an individual with one cancer is more likely to develop a second than he would be by chance alone.

Wallace[7] had one case of dual primary pulmonary cancer in 106 patients with multiple malignancy out of 3,006 patients with cancer. It is interesting to note that of 3 patients with a laryngeal cancer, 2 later developed and died from a bronchial cancer; one patient each had tracheal and breast tumors.

With respect to the rarity with which the lung is involved in multiple malignancy, Cahan and others[8] stated that the lung lesion was always the last to appear as it was so malignant—a second neoplasm would normally have time to show itself only when the first grows slowly, or is successfully treated.

McGrath and others[3] had 5 cases of two grossly visible carcinomata in the same or different lobes in a series of 87 cases. In another 25 cases, there were microscopic plaques of preinvasive or early invasive carcinoma both in close continuity with the main tumor and at such a distance from it as to be considered an independent lesion.

Spain and Parsonett,[9] by a multiple section technique, examined the bronchi of a 95-year-old woman. Although no gross lesion was seen, they found fortuitously several minute macroscopic cancers.

Several writers have discussed the potential of bronchial epithelium to develop multicentric sites of origin of cancer. Walter and Pryce[4] described appearances in epithelium adjacent to the tumor similar to that seen in Bowen's disease of the skin. They thought it probable that some squamous cell tumors started as intra-epidermal carcinomata. Auerbach and others[10] made an extensive microscopic study of all grossly normal areas from the tracheobronchial tree in 54 patients who died of bronchial carcinoma. They found separate areas of carcinoma in situ in 89 per cent of cases, and early invasive carcinoma in 9 per cent. They found carcinoma in situ alongside early invasive carcinoma, and suggested that the former was a stage prior to invasion. These authors point out one contradictory feature of this study in that the above changes were seen as commonly in the trachea as in the bronchi, but it has never been suggested that the incidence of tracheal carcinoma is increasing.

Hamilton and others[11] compared the bronchi of nonsmokers, smokers who did not develop carcinoma of the lung, and patients (opposite lung) dying of lung carcinoma by a multiple slide technique. Five types of epithelial changes were seen: basal cell hyperplasia, stratification, squamous metaplasia, transitional metaplasia, and an "intermediate" change. The commonest finding was basal cell hyperplasia, which was more extensive and was encountered in a significantly higher percentage of smokers' lungs, including those with carcinoma. The other changes showed only a slightly higher incidence in the above-mentioned groups. With the exception of basal hyperplasia, the changes described in bronchial epithelium had been observed in association with chronic inflammatory changes in the bronchial wall. However, the significant

difference in the incidence and extent of basal cell hyperplasia in cases of carcinoma of lung, and in smokers, could not be explained on the basis of inflammation.

CONCLUSION AND SUMMARY

In reporting 9 cases of dual primary carcinoma we would stress the need of recognizing the multiplicity of lung cancer.

It is interesting to note that adenocarcinoma was found in one case subsequent to polygonal cell carcinoma, and in another with oat cell carcinoma. This type of tumor, of course, is not usually associated with irritants.

The finding of two pulmonary shadows in a man of cancer age does not necessarily mean that they are metastases from a distant primary tumor, or that one is a primary lung tumor and the other is a metastasis from it.

It is suggested that the development of a new shadow, after an apparent cure of a previous primary cancer, may not indicate recurrence but may be a new tumor.

We should like to thank Dr. R. R. Wilson for the histologic specimens.

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INTRATHORACIC PHEOCHROMOCYTOMA

Dino Pampari, M.D., and Chiara Lacerenza, M.D.,***
Reggio Emilia, Italy

THE FIRST case of pheochromocytoma successfully operated was reported by C. H. Mayo in 1927,[1] and the first correct preoperative diagnosis was made by Pincoffs,[2] in 1929. In Italy, operated cases have been reported by Giovanni Forni,[3] Valdoni,[4] Pampari,[5] Pettinari,[3] Ferrandu,[6] Calzolari,[3] Ceccarelli,[3] Fasiani,[7] Mauri,[7] Biancalana (2 cases),[8] and Paolucci.[9] This multiplication of observations is undoubtedly attributable not so much to a real increase in the incidence of this tumor as to a more precise and enlarged knowledge of the disease, and even more to numerous pharmacologic tests which, since 1945, have been made available for the diagnosis of pheochromocytoma. Kvale and co-workers[10] reported recently that in the course of the last 11 years in the Mayo Clinic, 7,933 patients with hypertension have been submitted to pharmacologic tests and to the estimation of the urinary catecholamines, and these examinations permitted the exact diagnosis of 51 cases of pheochromocytoma. Numerous cases have been incidentally discovered in the course of a bilateral sympathectomy performed for hypertension. According to Graham,[11] in his over-all review of pheochromocytoma, Smithwick, in the course of 1,700 sympathectomies, has discovered 7 cases of pheochromocytoma. It would appear that, if all patients with hypertension in whom pheochromocytoma may be suspected were submitted systematically to pharmacologic tests, the identification of this tumor could be made much more frequently.

For the pharmacologic test, we possess various substances, some of which are particularly suitable for the study of pheochromocytoma which cause a persistent hypertension, others more suited for the study of patients in whom the tumor provokes a paroxysmal hypertension. Among the former is phentolamine, or Regitine (Grimson, Longino, Kernodle, and O'Rear[12] and Gifford, Roth, and Kvale[13]) and piperoxan, or benzodioxane (Goldenberg, Snyder, and Aranow[14]), which block the hypertensive effect of noradrenalin and epinephrine. Among the latter there is histamine (Roth and Kvale[15]), tetraethylammonium bromide (La Due, Murison, and Pack[16]), and methacholine chloride, or Mecholyl (Guarnieri and Evans[17]), which cause a brusque influx in the circulation of norepinephrine and epinephrine.

From the Surgical Department of the Arcispedale S. Maria Nuova, Reggio Emilia, Italy.
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*Reader in Surgical Pathology and Clinical Surgery at the University in Parma; Consult., Chief Surgeon at the Arcispedale S. Maria Nuova, Reggio Emilia, Italy.
**Anesthetist, Surgical Department of the Arcispedale S. Maria Nuova, Reggio Emilia, Italy.

To these tests should be added the estimation of the urinary pressure amines which has been recently introduced and which will show itself of particular merit, but is technically very complex. According to Euler and Floding,[18, 19] the secretion of noradrenalin, which in normal subjects reaches 20 to 40 mcg. in 24 hours, exceeds 100 to 200 mcg. in patients suffering from active pheochromocytoma. Less constant and less conspicuous is the increase in epinephrine secretion.

Such diagnostic means, having rendered the diagnosis of pheochromocytoma less difficult, have emphasized the difficulties inherent in the attempt at localization of the tumor. For establishing the site of the tumor, recourse has been had from the beginning to urography, to renal pneumography, and to retropneumoperitoneum. Recently, surgeons have tended to apply retropneumoperitoneum less and less frequently which, apart from its notable dangers, may give uncertain or fallacious results. They have limited themselves to a radiologic examination of the empty abdomen and to a urogram, and extended the surgical exploration in a systematic way to both sites of the kidneys which they approach by the transperitoneal route (Kvale, Roth, Manger, and Priestley[10]).

Such difficulties do not, however, beset the intrathoracic localization of the growth which is really the rarest of all and easily revealed by radiologic examination. It is the aim of this paper to describe a case of an intrathoracic pheochromocytoma (the seventh in the world literature) which had been diagnosed by us before the operation and in which the patient was then operated upon with full success.

CASE REPORT

V. O., 64 years old, was transferred to our department with the diagnosis of a neurogenic tumor of the posterior mediastinum.

For a year he had noticed a growing asthenia, a vague retrosternal pain, and dyspnea on exertion. His sleep became irregular, and often he would be overtaken during the night by anxiety, pulsating headache, and profuse perspiration. His body weight had undergone a notable reduction.

Examination revealed the obvious signs of arteriosclerosis, bradycardia (64 pulse beats per minute), and persistent hypertension, 180/120 mm. Hg. The electrocardiogram confirmed a sinus bradycardia and signs of left overloading. The laboratory tests were normal. Eye examination showed a hypertensive neuroretinitis of second degree.

Radiography of the thorax revealed the presence of an abnormal mass of homogeneous density the size of half a mandarin orange situated in the right costovertebral groove adjacent to the seventh and eighth thoracic vertebrae which appeared a little flattened by a process of erosion and compression. The lower edge of the mass merged into the shadow of the mediastinal pleura. The shadow of the heart was enlarged due to a dilatation of the left ventricle, and the walls of the aorta were partly calcified (Figs. 1 and 2).

The arterial blood pressure taken during one of the patient's nocturnal crises showed an increase to 220 mm. Hg, and, thus, the presence of a pheochromocytoma was strongly suspected. Thereupon the test with Regitine was carried out with a positive result (Fig. 3).

On April 17, having taken all precautions to cope promptly with a fall in arterial blood pressure, an anterolateral thoracotomy was performed in the bed of the right fifth rib. The tumor was covered by the mediastinal pleura and was embedded in the bodies of the seventh and eighth vertebrae. Explorative puncture showed that it was amply vascularized. After its removal (Fig. 4) a profuse hemorrhage occurred. There

Fig. 1.—Posteroanterior roentgenogram of chest shows a small oval mass projecting from the mediastinal shadow.

Fig. 2.—Lateral view shows mass in costovertebral region extending from seventh to eighth ribs.

followed an anxious alternation of improving and worsening of the heart action, which lasted for 1 hour and, at certain moments, required cardiac massage. After a transfusion of 1,800 c.c. of blood, introduced under pressure, and several administrations of Levophed, it was possible to raise the blood pressure to about 90 mm. Hg and eventually to bring about hemostasis. The operation lasted 2½ hours (Fig. 5). Undoubtedly, the cardiovascular symptoms produced by removal of the tumor were aggravated by the loss

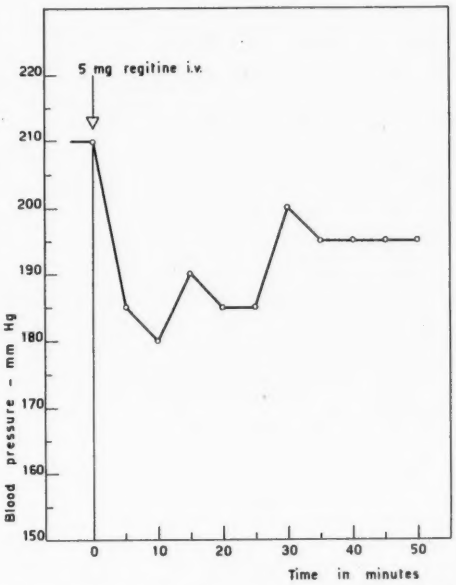

Fig. 3.—Changes in blood pressure resulting from the intravenous administration of Regitine (5 mg.).

Fig. 4.—The pathologic specimen.

of blood amounting to about 1,200 c.c. and by the arteriosclerosis. The blood pressure reached 120 mm. Hg in the afternoon and, in the following days, became stabilized around 140 mm. Hg. After 3 months, the blood pressure was maintained at 140 to 145 mm. Hg.

Histologic examination of the tumor showed the neoplastic tissue to be contained in a capsular sheath of sclerosed-hyalescent structure with sparse cellular elements and

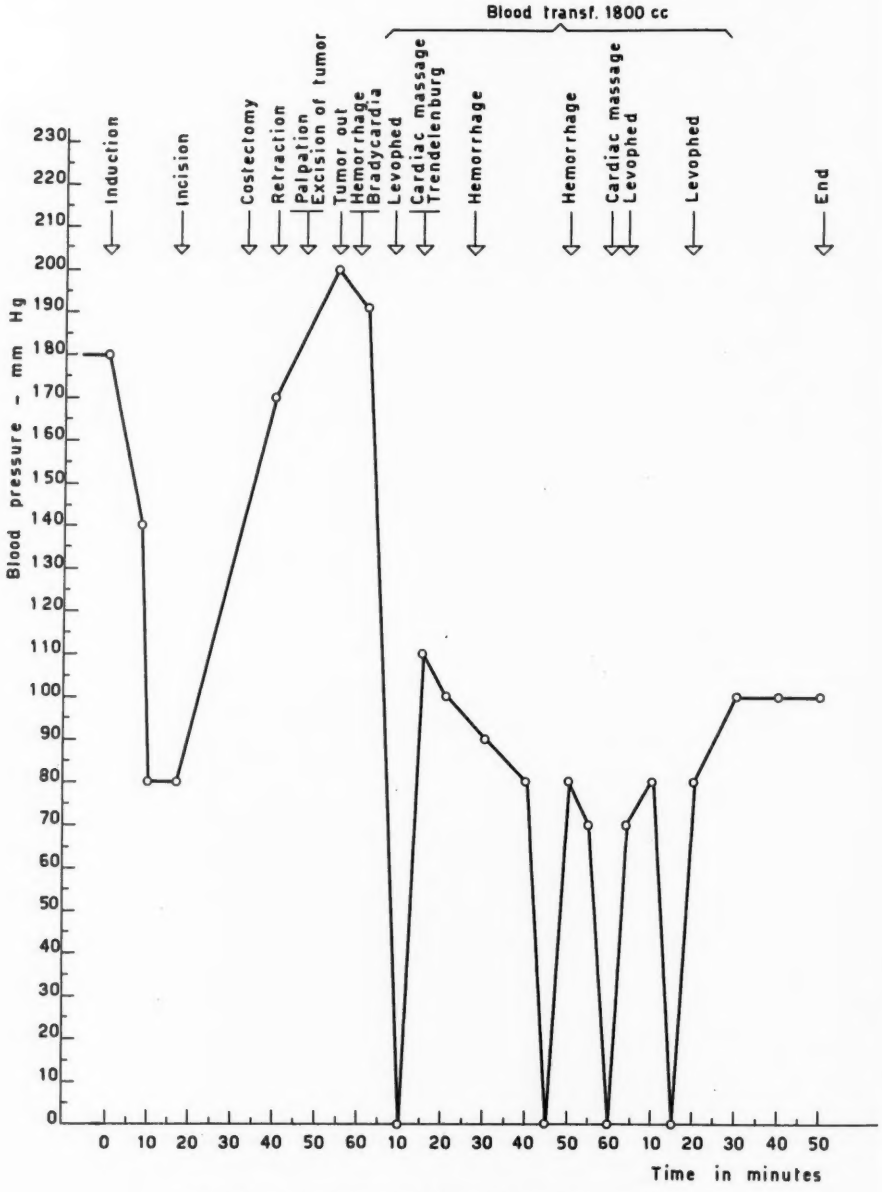

Fig. 5.—Changes in blood pressure during the operation.

Fig. 6.

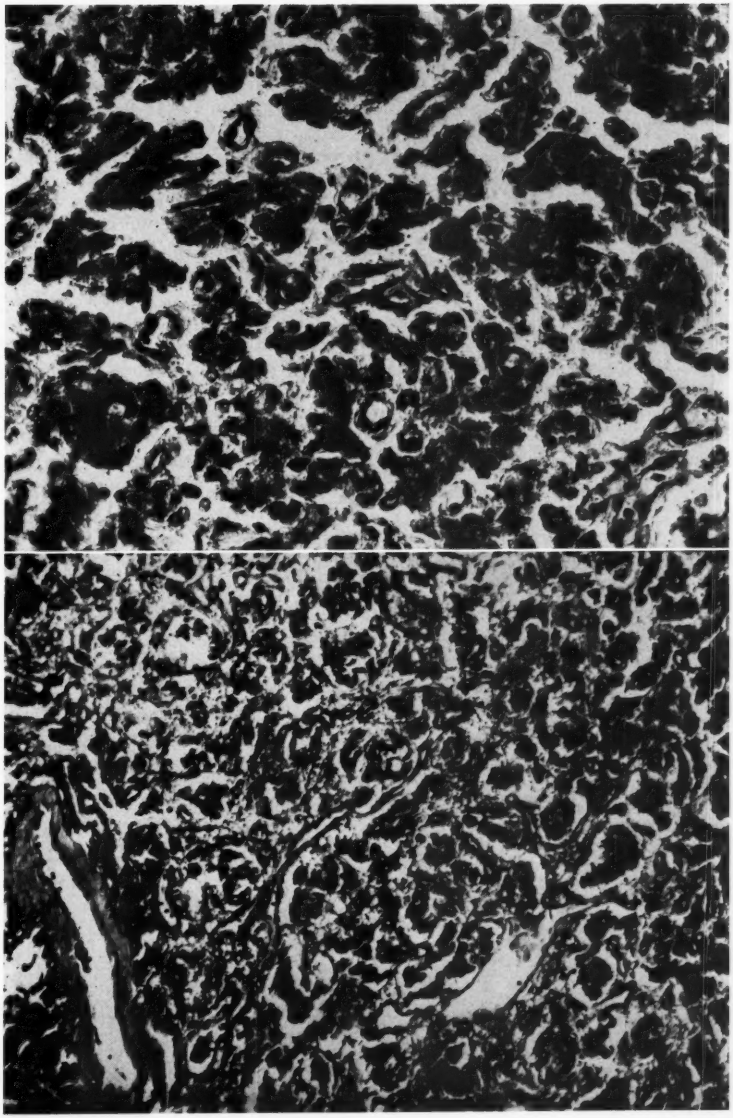

Fig. 7.

Fig. 6.—Photomicrograph of pheochromocytoma. The characteristic arrangement of tumor cells in lobules separated by capillaries is shown.

Fig. 7.—The chromaffin reaction (Bodian method).

traversed by vessels of indifferent aspect. The tumor tissue consisted of a collagenous stroma of variable development which, in some places, assumed a sclerosed and denser character, while in others it appeared quite scarce. The neoplastic cells which were arranged in columns or in alveolar formations, greatly differing in their size and shape, had a roundish or polygonal form and thin clear, slightly acidophilic cytoplasm, and indistinct contours. The nuclei had a rather rarefied chromatin network. Among these cells there could be discerned some which were conspicuous by their dimensions, and by their monstrous and gigantic appearance. Between the cell columns ran numerous capillary vessels which, in places, had an inspissated hyalinized wall with hypertrophic proliferating endothelial cells. In some zones extensive hemorrhagic infiltrations were visible. In a large area of the sections the presence of cartilaginous and bonelike tissue could be observed, consisting of inspissated lamellae and narrowed medullary lacunae. These tissues were, where they bordered the neoplasm, penetrated by neoplastic cells. The morphologic characteristics of the neoplastic cells, their arrangement in rows and alveoli, their intimate relation to capillaries, their similarity with medullary cells of the suprarenal glands, the presence of a capsule delimiting the growth, the benign morphologic aspect and clinical behavior of the tumor as well as its biologic behavior as a functioning growth, justified the diagnosis of pheochromocytoma (Fig. 6). The diagnosis was subsequently confirmed by the demonstration of the chromaffin reaction obtained with the method of Bodian (Fig. 7) (Professor Bini, Director of the Pathological Institute of the University in Parma).

In the literature there are 6 described cases of intrathoracic pheochromocytoma; 3 were found at necropsy while, in the remainder, the patients were successfully operated upon (Table I).

TABLE I

AUTHORS	SEX	AGE (YEARS)	LOCATION	PERSISTENT HYPERTENSION	PAROXYSMAL HYPERTENSION	RESULT
A. Cases of Intrathoracic Pheochromocytoma Diagnosed at Autopsy						
1. Miller (1924)	F	39	Right	?	?	
2. Philips (1940)	M	39	Left	-	Yes	
3. Wahl and Robinson (1943)*	M	4	Left	?	?	
B. Cases of Intrathoracic Pheochromocytoma Removed by Operation						
1. Maier (1949)	M	25	Left	Yes	-	Recovered
2. Overholt, Ramsay, and Meissner (1950)	M	16	Left	Normotensive		Recovered
3. Silvestrini, Genesi, Sachsel, and Costa (1957)†	F	39	Right	-	Yes	Recovered
4. Pampari and Lacerenza (1957)	M	64	Right	-	Yes	Recovered

*Sympathogonioma with mixed neuroblastic and pheochromoblastic elements, diffusely metastasized. Pheochromoblastic elements were present only in the primary growth.

†Operated upon by Fasiani.

SUMMARY

In every case of a posterior mediastinal tumor, associated with persistent or intermittent hypertension, the possibility of a pheochromocytoma should be kept in mind and the appropriate pharmacologic tests carried out to determine the diagnosis.

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PERIPHERAL LYMPHANGIOMA OF THE LUNG

F. G. Stephens, M.D., S. M. Roberts, M.D.,** and*
*M. W. Wolcott, M.D.,*** Augusta, Ga.*

In 1952, Worn[1] described a "cystic lymphangioma" within the pulmonary parenchyma and, in 1955, Giammalvo[2] presented a case of congenital lymphangiomatosis of the lung. We will present a third case of this rather rare lesion as illustrative of another type of solitary nodule to be considered in a differential diagnosis of single peripheral lesions of the lung.

REPORT OF A CASE

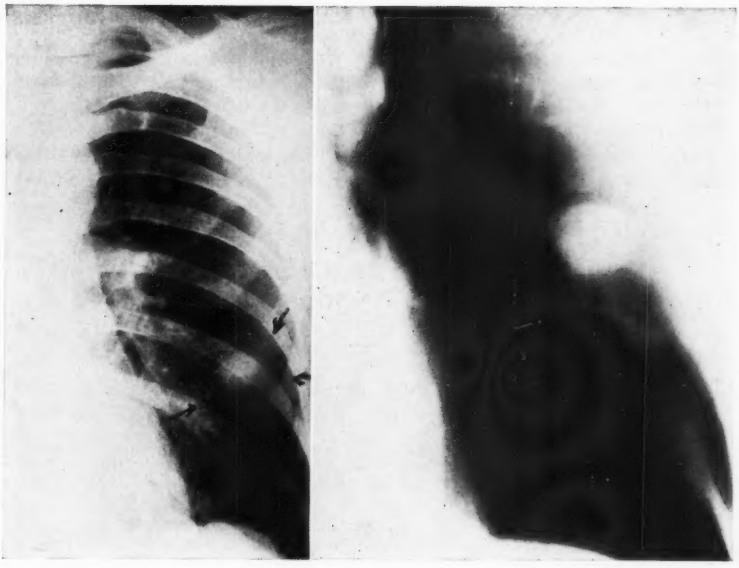
J. M. B., a 39-year-old white man, was admitted to this Veterans Administration Hospital on Jan. 25, 1957, as a transfer patient. He had been admitted previously to another facility on Sept. 11, 1951, for treatment of a duodenal ulcer, when a roentgenogram of the chest showed emphysematous blebs in the right apex but was otherwise normal. In 1956, a routine chest film (Fig. 1, *A*) had revealed an increased density, approximately 2.5 by 3.0 cm. in the left lung. The patient thought that he had had a slight increase in cough, but denied having had hemoptysis, dyspnea, fever, or weight loss.

Physical examination, which in general was negative, revealed a well-developed white man without dyspnea, orthopnea, or cough. Blood pressure was 140 systolic, 90 diastolic, pulse rate 80, and temperature was normal.

All laboratory examinations, including an electrocardiogram, were within normal limits. A planigram (Fig. 1, *B*) showed a lesion in the left lower lung field, extending from 7 through 15 cm. levels, which was well circumscribed, ovoid, smooth in outline, and of uniform fluid density. Skin tests for histoplasmosis, coccidioidomycosis, and blastomycosis were negative. Purified protein derivative in first strength was negative, reaction to second strength was 4 plus. Bronchoscopic examination was negative. Papanicolaou smears taken at bronchoscopy revealed no tumor cells. After a review by the tumor board, exploratory thoracotomy was recommended.

At operation the left chest was entered by means of a standard posterolateral incision through the bed of the fifth rib. Near the anterior aspect of the major fissure was a cyst, approximately 2 cm. by 2½ cm. This was in the fissure, covered by visceral pleura, but by palpation there appeared to be no connection with the major vascular or bronchial systems. Both by inspection and palpation, the entire lung and hilar area appeared normal. The cyst was readily removed by blunt and sharp dissection, without significant air leak, and with very little bleeding. The pleural space was drained by two catheters, followed by routine closure. The postoperative course was uneventful.

From the Veterans Administration Hospital, Augusta, Ga.
Received for publication March 6, 1958.
*Chief, Laboratory Service, VA Hospital, Augusta, Ga.
**Chief, Radiology Service, VA Hospital, Augusta, Ga.
***Chief, Thoracic Service, VA Hospital, Augusta, Ga. Present address: Chief, Surgical Service, VA Hospital, Coral Gables, Fla.



A. *B.*

Fig. 1.—*A*, Roentgenogram shows a well-circumscribed lesion in the left lower lung field, of uniform density, with fine threadlike strands radiating from the periphery. *B*, A planigram shows the lesion at the 12 centimeter level.

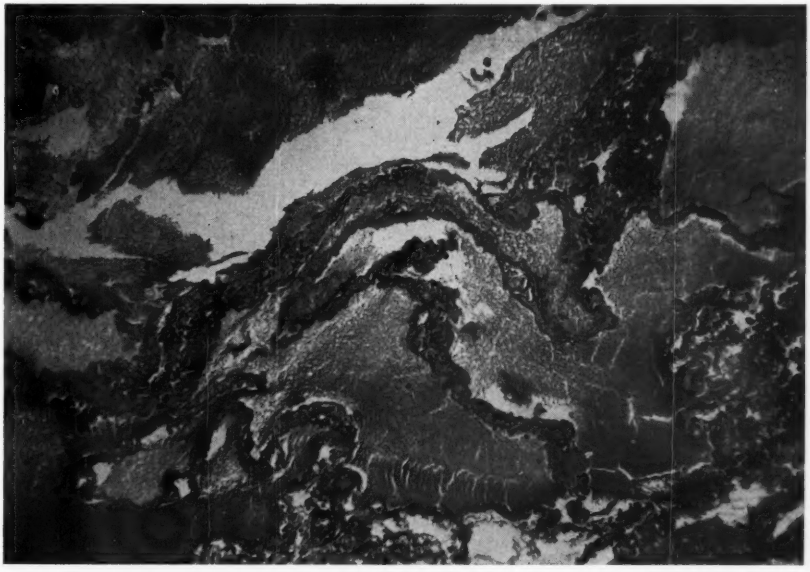


Fig. 2.—Microscopically the lesion showed thin walls and cystic spaces, some containing acidophilic precipitate.

Pathologic examination: The entire specimen was a fluctuant thin-walled cystic mass, 1.8 by 0.4 cm., completely encapsulated. To obviate loss of contents, the specimen was embedded without sectioning. Microscopically (Fig. 2), the periphery was composed of loose connective tissue. Irregular trabeculae extended from this and interlaced within the mass. These trabeculae were lined by flattened cells. The spaces between the strands were irregular and often contained an eosinophilic precipitate. Lymphocytes were noted in these spaces and, occasionally, lymphocytes and granulocytes occurred in small aggregates. Occasionally a small focus of lymphocytes was noted in the connective tissue of the walls.

SUMMARY

A case of lymphangioma of the lung is presented. This lesion may be due to mechanical blocking of the lymphatics with focal peripheral dilatation. In a young individual, a congenital defect or variation may be the pathogenesis of the lesion.

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ANTHRACO-SILICOSIS PRESENTING AS A SOLITARY PULMONARY LESION

W. Clayton Davis, M.D., and Walter T. Snow, M.D.,** Man, W. Va.*

THE PURPOSE of this paper is to present a case of a solitary pulmonary lesion different from any previously encountered by the authors. No similar case has been found in the available literature.

CASE REPORT

B. B., a 59-year-old white man, reported to the Out Patient Department of the Man Memorial Hospital with complaints of weakness and epigastric distress. As part of his study, chest radiographs were obtained and showed a rounded area of increased density, 4 cm. in diameter, in the posterior segment of the right upper lobe adjacent to the oblique fissure (Fig. 1, *A* and *B*). After surgical consultation, the patient was admitted to the hospital for study regarding this pulmonary lesion. He gave a 3-year history of an involuntary squint, entirely intermittent in nature. Previously he had been studied by a neurosurgeon who felt that the abnormality could not be based on any organic neurologic defect. He had had no operations or previous major illnesses. He never used tobacco of any kind. There was no recent change in weight. There was no family history of malignancy. Except for the noted involuntary squint, the physical examination was entirely normal.

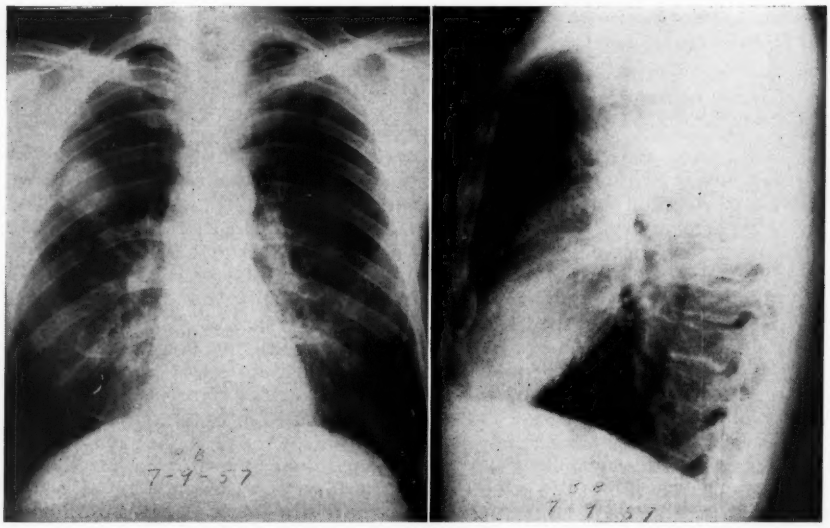
Because of the possibility of this being a primary or secondary malignant lesion, numerous laboratory studies were performed. Complete blood count, urinalysis, serum bilirubin, thymol turbidity, prothrombin time, cephalin flocculation, serum amylase, glucose tolerance, gastric analysis, and nonprotein nitrogen were all within normal limits. Radiologic studies including a gastrointestinal series, excretory urogram, bone survey, barium enema, and gall bladder visualization were normal. Retrograde pyelogram and cystoscopy were also normal.

Because of the undiagnosed pulmonary lesion in the posterior segment of the right upper lobe, bronchoscopy and exploratory thoracotomy were performed under general endotracheal anesthesia on July 30, 1957. Bronchoscopy was normal. A right posterolateral thoracotomy incision was made through the fourth intercostal space. Numerous fibrinous adhesions were divided throughout the entire right pleural space. All structures were normal except the right upper lobe where a lesion was noted occupying the entirety of the posterior segment with fixation to the interlobar fissure. The pulmonary lesion was hard, multilocular and multinodular. There was puckering of the visceral pleura. There was a gross appearance of malignancy. A right upper lobectomy was performed (Fig. 2). Frozen section diagnosis was a "benign infiltrate." Because of an extremely poor interlobar fissure and a purposeful sacrifice of portions of the right middle lobe, a middle lobectomy was then performed.

The patient made an uneventful postoperative recovery and was discharged from the hospital on his seventh postoperative day. Follow-up examinations (Fig. 3, *A* and *B*) have been performed. He returned to full work as a coal miner 5 weeks after operation. He tolerates his work well, reports no dyspnea, and has no new complaints.

From the Man Memorial Hospital, Man, W. Va.
Received for publication March 12, 1958.
*Associate Chief of Surgery, Man Memorial Hospital, Man, W. Va.
**Chief of Radiology, Man Memorial Hospital, Man, W. Va.

Pathologic Report.—Specimen consists of the upper lobe of the right lung which showed near its periphery, adjacent to the surface in contact with the middle lobe, a round hard lesion measuring approximately 4 by 5 cm. On section it is found to contain approximately 15 c.c. of fluid with small black particles. The cut surface is jet black and reveals an occasional small cystic space,



A. *B.*

Fig. 1.—*A* and *B*, Preoperative chest radiographs of Case 1.

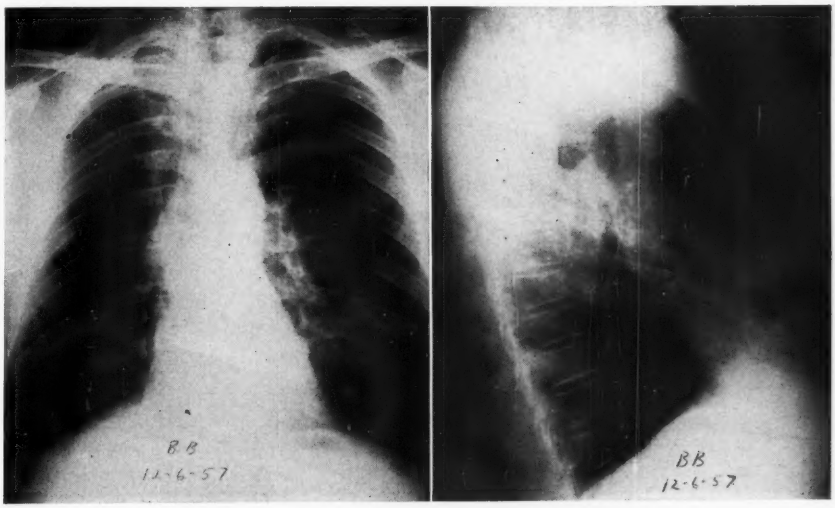
Fig. 2.—View of nodule resected in right upper lobe of Case 1.

the largest measuring approximately 0.8 cm. in diameter. A large amount of black material is found in the bronchus leading to the lesion. The mass is fairly well circumscribed and solid. There is a line of sharp demarcation between the mass and the surrounding compressed lung. The second specimen consists of a resected middle lobe. Near one edge, it appears more solid and more anthracotic than is usually encountered even in this geographic region.

Microscopic sections reveal the solid portion of the tumor to be composed of connective tissue which is heavily pigmented throughout. In some areas, there is calcium deposited around the small cystic spaces described in the gross examination. The walls of these spaces are composed of dense scar. In other areas, there are cholesterol flecks. The blood vessels remain intact in most areas. The bronchi have for the most part disappeared. In the portion of the lung not involved in the tumor mass, there is moderate anthracosis.

Diagnosis.—Anthraco-silicotic nodule, posterior segment, right upper lobe.

Review of the slides by Dr. V. E. Martens, Director of Laboratories, National Naval Medical Center, was reported as showing black anthracotic pigment and, under the polarizing microscope, refractile bodies which are typical of anthraco-silicotic nodules.



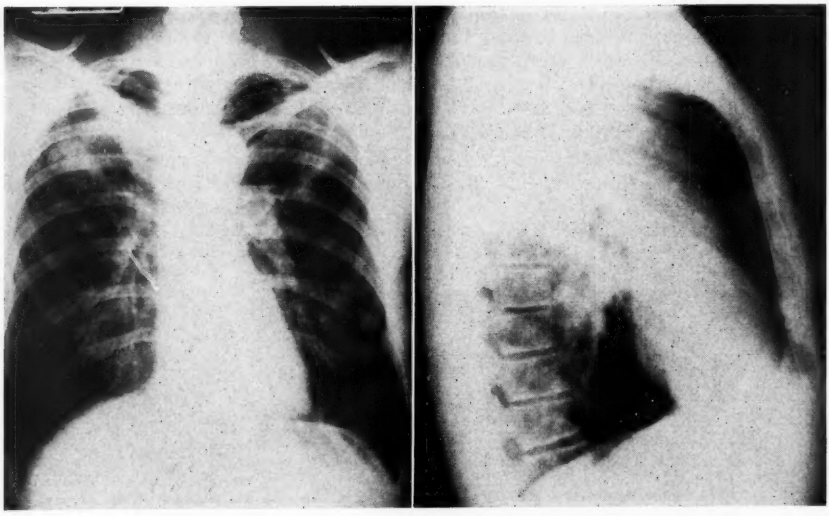
A. *B.*

Fig. 3.—*A* and *B*, Three months postoperative chest radiographs of Case 1.

DISCUSSION

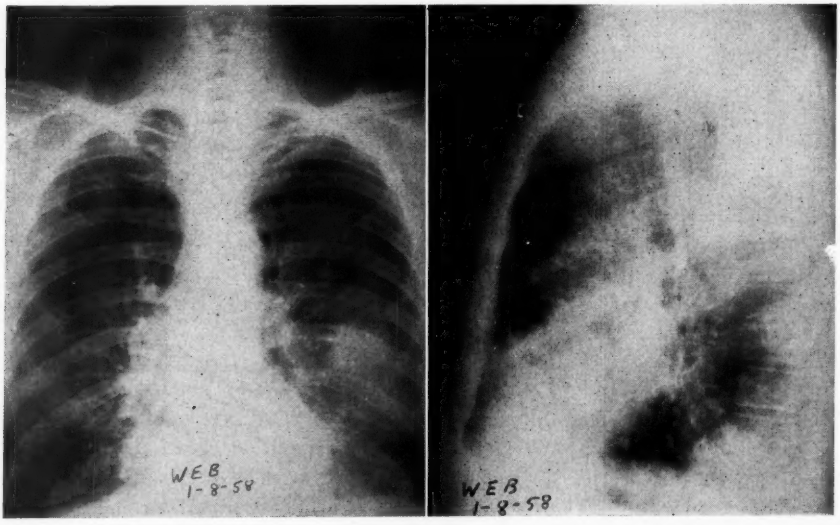
The diagnosis of solitary lesions in the lung is a subject which has received much attention in the literature. In December, 1956, Davis and colleagues[1] reviewed their 215 cases and added them to an analysis of reported series totaling 1,203 cases. No mention is made in any of these reports of a lesion due to any of the pneumoconioses. Pneumoconiosis is not included in the differential diagnosis of solitary pulmonary shadows in the Outline of Radiographic Diagnosis compiled by the Resident staff at the University of Michigan.[2]

Recently the authors have encountered 2 men with problems similar to the case presented here. The diagnosis of anthraco-silicosis could be made radiologically (Figs. 4, *A* and *B*, and 5, *A* and *B*) because of multiple nodules. There were more definite diagnostic criteria of pneumoconiosis than in our presented case in which the final diagnosis was not considered preoperatively. It seems logical, therefore, that an addition should be made to the classification of pneumoconiosis presented in Table I.



A. *B.*

Fig. 4.—*A* and *B*, Coal miner with definite radiologic diagnosis of pneumoconiosis showing a large, fairly discrete mass in the posterior segment of the right upper lobe. Case 2.



A. *B.*

Fig. 5.—*A* and *B*, Coal miner with radiologic evidence of pneumoconiosis with large, fairly discrete lesions in both lower lobes. Case 3.

TABLE I. INTERNATIONAL CLASSIFICATION PNEUMOCONIOSIS

Simple Pneumoconiosis:	
Category 1.	In these radiographs a small number of opacities may be seen in at least two anterior rib spaces extending over not more than half of the medial two thirds of the lung fields.
Category 2.	In these radiographs, opacities extend over more than half of the medial two thirds of the lung fields but are sparse or absent in the lateral third.
Category 3.	In these radiographs, numerous opacities extend over the whole of both lungs including the lateral third, although they may be sparse or absent above the clavicle.
Complicated Pneumoconiosis:	
	Complicated pneumoconiosis or pneumoconiosis with coalesence or massive shadows.
Category A.	In these films opacities more than 1 cm. in diameter may be seen in one or more areas, commonly coalescent, but not constituting a massive shadow of even density.
Category B.	In these films one or more massive shadows are present, extending over less than the equivalent of three anterior rib spaces on either side.
Category C.	In these films large massive shadows of uniform density extend over the equivalent of three or more anterior rib spaces on either side.
Category D.	In these radiographs, one of the more massive shadows is presented associated with gross distortion of the pulmonary anatomy. The massive shadows may of themselves be such as to be classified A, B, or C in the absence of distortion.

Since nowhere in the available literature and classifications of pneumoconiosis is there mention of isolated solitary lesions, a new category should be added. The authors propose the term "Atypical Lesions" which could include solitary anthraco-silicotic lesions occurring in lungs which otherwise show only minimal or even equivocal findings of pneumoconiosis, and solitary lesions occurring in lungs which show findings more diagnostic of pneumoconiosis. We feel that future cases, especially in our geographic area, will enlarge this section of the classification. This seems especially probable since 3 such cases have been encountered in less than 6 months.

SUMMARY

A case of a solitary pulmonary lesion due to anthraco-silicosis is presented. No mention of a similar entity has been found in either the literature on solitary pulmonary nodules or that on pneumoconiosis.

It is proposed that this possibility be added to the differential diagnosis of solitary pulmonary nodules especially in geographic areas in which pneumoconiosis is encountered.

It is also proposed that the classification of pneumoconiosis be enlarged to include a category of "Atypical Lesions," such as the cases mentioned in this report.

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THE SURGICAL TREATMENT OF PULMONARY TUBERCULOSIS COMPLICATED BY PULMONARY INSUFFICIENCY

David V. Pecora, M.D., Ray Brook, N. Y.

IN EVERY clinic engaged in the treatment of pulmonary tuberculosis there are many patients with pulmonary insufficiency. Of these, many can be cured with the aid of surgery, provided every effort is made to preserve function. Unfortunately, preservation of function is not always compatible with cure of tuberculosis. On the contrary, efforts to preserve function may actually have an adverse effect upon the patient's disease. Because of this, choice of procedure may be difficult. It is the purpose of this study to review our experience in the hope of facilitating such decisions by determining the indications and limitations of several procedures which we have employed.

MATERIALS AND METHODS

Three types of surgery have been employed at the Ray Brook State Tuberculosis Hospital in the treatment of patients with limited pulmonary function: plombage thoracoplasty, local cavitary resection (cavernectomy), and Monaldi drainage.[1]

Plombage thoracoplasty is employed with the intention of collapsing cavitary disease and as little functional lung as possible. Polyethylene beads are inserted into the subcostal space during the first stage. Beads are later removed only when infection occurs or resection is performed.

Cavernectomy consists of the removal of the cavity and the adjacent dense disease. In many patients with smooth "healed" cavities, who have received long-term preoperative combined antituberculous drug therapy, it has been possible to remove little more than the cavity wall (Fig. 1). In other patients with appreciable dense pericavitary disease, it has been necessary to perform segmental resection, or, less frequently, lobectomy. No attempt is made to remove all noncavitary disease and, in almost all instances, diseased lung has been transected.

Monaldi cavitary drainage is performed essentially as described by Woodruff and associates.[2] When the parietal and visceral pleura is known to be adherent, no preliminary rib resection is performed. Otherwise a small segment of rib and periosteum is resected and the formation of adhesions is encouraged by applying tincture of iodine to the parietal pleura in the rib bed. Every effort is made to avoid crossing pulmonary fissures when inserting the

From the Ray Brook State Tuberculosis Hospital, Ray Brook, N. Y.
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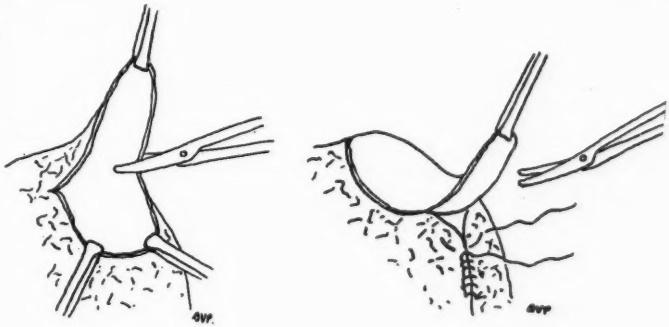
catheter. Lower lobe cavities are approached from the axilla or posteriorly.[3] In a number of instances in which local resection of cavitary disease has proved impossible at the time of exploratory thoracotomy, for reasons such as the proximity of important hilar structures, a small incision is made into the cavity and the tip of a 16 F. double-eye catheter is inserted. The opening is then closed about the catheter with several purse-string sutures of atraumatic chromic 2-0 catgut. The last of these sutures is tied about the catheter. Suction is applied to the catheter with a bulb syringe to check for leaks, as it is important that the closure be airtight. The other end of the catheter is brought out of the chest through a stab wound in the axilla. Immediate expansion of the lung is ensured by inserting two 28 F. double-eye rubber catheters into the pleural cavity. The tip of one is sutured by a single stitch to the anterior apical pleura, and the tip of the other is led to the base posteriorly. These catheters are also brought out through stab wounds in the axilla. As soon as possible, about 40 cm. water suction is applied to the catheters in the pleural space and 20 cm. to the intrapulmonary cavity. The pleural tubes are removed usually in about 1 week. Suction is generally maintained continuously upon the cavernostomy tube for about 1 month. Following this, the patient is allowed to walk about at intervals with the tube clamped.



A. *B.*

Fig. 1.—Method of locally excising a "healed" tuberculous cavity.

A, The cavity is unroofed. Bleeding is controlled with Allis clamps.

B, The floor of the cavity is excised with a small amount of adjacent lung tissue. The lung is progressively sutured with either interrupted 4-0 silk or continuous 2-0 atraumatic chromic catgut. Usually two layers of the latter suture are used.

Cavernostomy tubes are changed about once a month. Progress of cavity closure is determined at intervals by injecting iodized oil into the tube. Pneumoperitoneum is frequently administered as a supplement to tube cavernostomy. It is our present policy to remove the drainage tube after the sputum and cavity drainage have been negative for tubercle bacilli by culture for about 10 months, provided the cavity has closed. Whenever possible, combined antituberculous drug therapy is administered for at least a year concomitantly with cavernostomy. If only single drug coverage is available, drug therapy is not started until the cavity has been obliterated.

In order to determine the effect of residual disease upon the prognosis following local resection of cavitary lesions, Tables I and II have been compiled. To provide sufficient material for analysis, all of the resections for pulmonary tuberculosis performed at Ray Brook from January, 1950, to January, 1957, were reviewed. Resections which were not covered by antituberculous drugs and those concerning which sufficient information was not available were eliminated. Since it has been shown elsewhere[4, 5] that postoperative tuberculous complications may be influenced by the presence of tubercle bacilli at the time of surgery, and by the number of drugs administered, this information is included in the tables. Both early (postoperative spread of disease, empyema, and wound infection) and late (bacterial and roentgenographic relapse) tuberculous complications are listed together. A maximum of one tuberculous complication is attributed to each operation. The patients who had resections performed are divided into three groups according to the estimated amount of disease remaining after surgery: (1) those with no residual palpable disease on the side operated upon and no contralateral disease disclosed by roentgenogram; (2) those with "appreciable residual disease," that is, residual disease involving the equivalent of one half or more of one lung volume; and (3) an "intermediate group."

TABLE I. TUBERCULOUS COMPLICATIONS IN PULMONARY RESECTIONS PERFORMED UPON PATIENTS WITH CULTURABLE TUBERCLE BACILLI IN THE SPUTUM OR RESECTED TISSUE

NUMBER OF DRUGS WITH RESECTION	TOTAL		NO RESIDUAL DISEASE		"INTERMEDIATE GROUP"		"APPRECIABLE DISEASE"	
	COMPLICATIONS	NO COMPLICATIONS	COMPLICATIONS	NO COMPLICATIONS	COMPLICATIONS	NO COMPLICATIONS	COMPLICATIONS	NO COMPLICATIONS
One	20 (40%)	31 (60%)	1 (22%)	7 (88%)	6 (35%)	11 (65%)	13 (50%)	13 (50%)
Two or more	10 (14%)	64 (86%)	2 (9%)	20 (91%)	4 (20%)	16 (80%)	4 (13%)	28 (87%)
Total	30 (24%)	95 (76%)	3 (10%)	27 (90%)	10 (27%)	27 (73%)	17 (29%)	41 (71%)

TABLE II. TUBERCULOUS COMPLICATIONS IN PULMONARY RESECTIONS PERFORMED UPON PATIENTS WITH SPUTUM AND RESECTED TISSUE FREE OF CULTURABLE TUBERCLE BACILLI

NUMBER OF DRUGS WITH RESECTION	TOTAL		NO RESIDUAL DISEASE		"INTERMEDIATE GROUP"		"APPRECIABLE DISEASE"	
	COMPLICATIONS	NO COMPLICATIONS	COMPLICATIONS	NO COMPLICATIONS	COMPLICATIONS	NO COMPLICATIONS	COMPLICATIONS	NO COMPLICATIONS
One	2 (13%)	13 (87%)	0	5 (100%)	0	3 (100%)	2 (29%)	5 (71%)
Two or more	3 (1%)	284 (99%)	0	95 (100%)	2 (2%)	109 (98%)	1 (1%)	80 (99%)
Total	5 (2%)	297 (98%)	0	100 (100%)	2 (2%)	112 (98%)	3 (3%)	85 (97%)

Whenever drug therapy is discussed, only "effective" drugs are included, that is, only those drugs to which the patient's organisms were sensitive. Organisms are considered sensitive to streptomycin, para-aminosalicylic acid, or isoniazid, if they did not grow in the presence of 10 mcg. of the first two drugs or 5 mcg. of the last drug, respectively. Details of the bacteriological methods employed have been presented elsewhere.[5] Organisms are considered sensitive to viomycin, cycloserine, pyrazinamide, or tibione if the patient had not previously received them.

RESULTS

From the functional aspect, plombage thoracoplasty has much merit. If little functional lung is collapsed there is little decrease in ventilation. Moreover, during the early postoperative period, function is approximately as good as it is several months later.[6] Unfortunately this procedure has not cured many, in our experience. Between July, 1954, and July, 1957, this procedure was employed on 18 occasions at Ray Brook. Sixteen of these were on patients with far-advanced disease and 2 on patients with moderately advanced disease.* Of the 18, only 5 procedures succeeded in closing cavities. Of 13 procedures performed upon patients with infectious sputum, only 2 succeeded in converting the sputum to negative. Of the 5 patients in whom cavity closure was achieved, only 2 had infectious sputum at the time of surgery. The important role of antituberculous drug therapy is indicated by the fact that 4 of the 5 patients in whom cavity closure was achieved received concomitant drug therapy, while 9 of the 13 patients in whom cavity closure failed did not receive antituberculous drug therapy.

Surgical complications have been infrequent following this procedure. There have been no early postoperative spreads of disease. Two infections of the subcostal space occurred. Tubercle bacilli were cultured from one and *Bacillus proteus* from the other. Both of these healed promptly following removal of the foreign material and establishment of drainage. One patient died approximately 2 months postoperatively of cor pulmonale. Another patient died 6 months following surgery of hemorrhage from a contralateral cavity. Two patients died as a result of later surgery, one of a cardiac arrest during pulmonary decortication, and another as a result of attempted resection at another institution.

It is realized that these poor results reflect the extensive disease present. Nevertheless, since some of these patients were later successfully treated by resection of the cavity-bearing area, it would appear that the latter procedure is preferable if it is believed that the patient can tolerate it. For this reason it is our present policy to perform plombage thoracoplasty only when we believe resection would involve a great risk.

The ventilatory changes which occur with pulmonary resection have been reviewed elsewhere.[6] Briefly, there may be little permanent change if only nonfunctional lung is excised. The greatest disadvantage of resection lies in the often extreme temporary depression in ventilation which occurs in the early postoperative period.

The concept of treating pulmonary tuberculosis by attempting to obliterate cavitary disease is certainly not new. Early in our experience with resection for pulmonary tuberculosis,[7] it seemed that local excision of cavitary disease might yield good results. However, it soon became evident that results were not uniformly good, especially when appreciable amounts of residual disease remained. In Tables I and II, an attempt is made to determine the factors which influence the results of local cavitary excision. From Table II,

*National Tuberculosis Association classification.

it will be noted that tuberculous complications are uncommon in those patients who have had sufficient antituberculous drug therapy to render them noninfectious. All of these were late complications. On the other hand, Table I indicates a relatively high incidence of tuberculous complications in the patients who had infectious specimens or sputum at the time of surgery. In both tables the superiority of multiple drug therapy is apparent, although less so in the patients with noninfectious disease (Table II). Also, in both tables, the unfavorable effect of residual disease is apparent, although less so in the noninfectious patients (Table II). It would appear that the amount of residual disease influences results most unfavorably when only one antituberculous drug is given and when the sputum (or resected tissue) contains culturable tubercle bacilli. Conversely, the amount of residual disease is of only slight importance when the sputum and resected tissue do not yield culturable tubercle bacilli and when 2 or more antituberculous drugs are administered.

Six patients, included in Tables I and II, died of the following causes: cardiac arrest, postoperative intrapleural hemorrhage, hepatic necrosis (presumably the result of toxicity to pyrazinamide), pulmonary edema, coronary occlusion, and cirrhosis of the liver.

Monaldi cavernostomy can be performed by the percutaneous route with little effect upon pulmonary function. Of course, when it is performed at open thoracotomy, there follows a temporary depression in ventilation similar to that which occurs after pulmonary resection. Cavernostomy has yielded variable results, depending upon a number of factors. A review of 32 procedures performed upon 28 patients at Ray Brook between January, 1946, and July, 1957, reveals that all of the patients had infectious sputum at the time of Monaldi cavernostomy and in only 13 was a noninfectious state achieved. Of 15 procedures performed without concomitant antituberculous drug therapy, 14 failed to achieve negative cultures of the sputum. In the fifteenth case, the sputum became negative microscopically. Of 10 patients who received single antituberculous drug therapy, or less than 6 months of combined drug therapy, 6 developed noninfectious sputum. All 7 patients who received combined antituberculous drug therapy for over 6 months developed noninfectious sputum.

The value of posterolateral thoracoplasty as an adjunct to Monaldi cavernostomy is not evident. In this series, posterolateral thoracoplasty was performed on 19 occasions, following which the sputum became noninfectious in 8 instances. One additional patient developed microscopically negative sputum. Of the 13 instances in which posterolateral thoracoplasty was not performed, 5 patients developed noninfectious sputum. Neither these data nor Monaldi's experience[8] indicate that thoracoplasty is necessary in many cases.

In this group of patients, complications have been limited to bleeding which was transient, except in one instance which terminated fatally. During bleeding episodes, suction is discontinued temporarily and the patient is encouraged to clear the bronchial tree by coughing gently. Few patients who

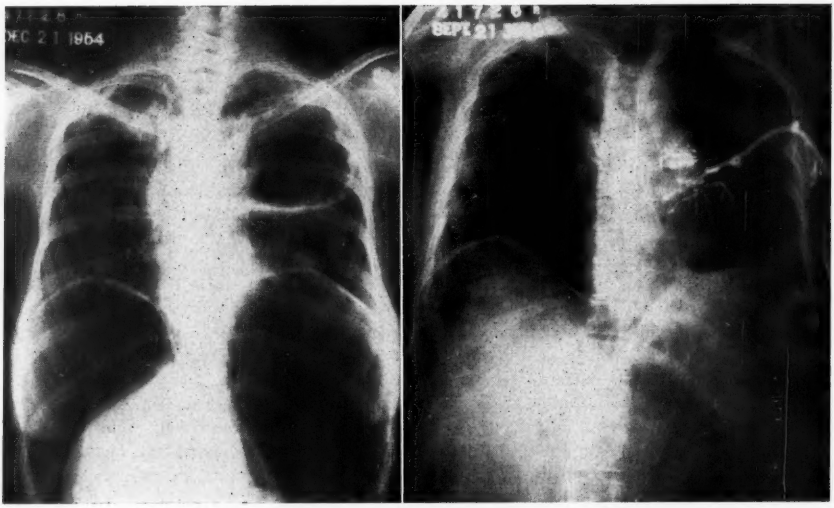
have received concomitant antituberculous drugs have experienced this complication. Of the 28 patients treated by Monaldi cavernostomy, 7 are known to be dead. Six of these patients had failed to achieve noninfectious sputum; the other died of bronchogenic carcinoma.

REPRESENTATIVE CASES

CASE 1.—R. R., a 26-year-old woman, was admitted to Ray Brook State Tuberculosis Hospital on Nov. 15, 1954, with sputum containing tubercle bacilli resistant to streptomycin, para-aminosalicylic acid, and isoniazid. A roentgenogram of the chest revealed disease throughout both lung fields and large cavities bilaterally (Fig. 2, *A*). The patient was extremely ill and dyspneic. Pneumoperitoneum had been initiated prior to admission and was continued until March 16, 1957. On June 7, 1955, under local 1 per cent procaine anesthesia, a small segment of the left fourth rib with periosteum was removed through an incision in the axilla. The underlying pleura was wiped with tincture of iodine to create adhesions. On June 21, 1955, under fluoroscopic guidance with the aid of a trocar, a tube was inserted into the underlying pulmonary cavity through a small stab wound over the previously resected fourth rib. The cavity rapidly decreased in size and on Oct. 20, 1955, and again on Sept. 21, 1956 (Fig. 2, *B*), it could not be demonstrated by injection of iodized oil through the catheter. On June 8, 1956, pyrazinamide, 1 gram 3 times a day, and viomycin, 1 gram every 12 hours 2 days a week, were started. These drugs were continued until July 19, 1957. Vital capacity on June 22, 1956, was 1,300 c.c. total and 1,100 c.c. in 3 seconds. On June 29, 1956, right upper and middle lobectomy were performed, removing a large shaggy cavity which occupied both lobes. The postoperative course was uncomplicated and the sputum became noninfectious. The patient was discharged from the hospital on Jan. 18, 1958. Vital capacity on that day was 1,700 c.c. total and 1,400 c.c. in 3 seconds.

CASE 2.—B. P., a 32-year-old woman, was admitted to Ray Brook State Tuberculosis Hospital for the second time on Feb. 2, 1957. Her sputum contained tubercle bacilli which were resistant to 10 mcg. of para-aminosalicylic acid and 5 mcg. of isoniazid. Roentgenograms of the chest revealed diffuse disease in the left lung with cavitation in both lobes and a small amount of disease in the right lung. Vital capacity was 1,600 c.c. total and 1,000 c.c. in 3 seconds. On July 12, 1957, pyrazinamide, 1 gram three times a day, and cycloserine, 250 mg. every 12 hours, were substituted for para-aminosalicylic acid and isoniazid therapy which the patient had been receiving. On July 24, 1957, streptomycin was substituted for cycloserine. On July 22, 1957, a left exploratory thoracotomy was performed. Two cavitary areas were identified, one in the apical-posterior segment of the upper lobe and one deep within the lower lobe. The lower lobe cavity was incised, revealing necrotic and purulent contents. It was obvious that this cavity could not be resected without sacrificing the whole lower lobe. Therefore, a 16 F. catheter was placed into the cavity and the incision was closed tightly about the catheter with sutures of 2-0 atraumatic chromic catgut. One suture was tied about the catheter. The apical-posterior segment and a wedge of the anterior segment of the upper lobe were then resected. When this specimen was incised it revealed two cavities, one with a smooth glistening lining and one with a shaggy purulent membrane. Cultures of the former yielded no tubercle bacilli; those of the latter, many tubercle bacilli. Pneumoperitoneum was started on July 23, 1957. There were no postoperative complications. Following surgery, the patient's sputum became noninfectious. On Oct. 1, 1957, injection of iodized oil into the cavernostomy cavity failed to reveal evidence of cavitation, although a good bronchogram was obtained. Vital capacity on Jan. 24, 1958, was 1,700 c.c. total and 1,500 c.c. in 3 seconds.

CASE 3.—R. M., a 34-year-old man, was admitted to Ray Brook State Tuberculosis Hospital on Feb. 18, 1957, with tubercle bacilli resistant to streptomycin and para-aminosalicylic acid in his sputum. Chest roentgenograms revealed scattered noncavitary disease



A. *B.*

C.

Fig. 2.—Roentgenograms of Case 1.

A, Appearance of disease before surgical treatment.

B, After a period of Monaldi drainage, no cavity is visible when iodized oil is injected into the catheter.

C, Roentgenogram following right upper and middle lobectomy.

involving the upper half of the right lung and two large cavities in the left upper lung field. In addition, there was scattered noncavitary disease in the remainder of the left lung. Fluoroscopy revealed evidence of obstructive emphysema bilaterally, worse on the left side. Vital capacity was 2,600 c.c. total and 2,000 c.c. in 3 seconds. On Oct. 18, 1957, viomycin, 1 gram every 12 hours 2 days a week, and pyrazinamide, 1 gram 3 times a day, were started. Isoniazid was not administered since the patient had been receiving the drug continuously for a prolonged period and it was thought possible that the patient's organisms might have developed resistance to the drug. On Oct. 25, 1957, a left pulmonary decortication and left upper lobectomy were performed. In addition, a large cavity with a smooth glistening membrane was removed from the lower lobe as illustrated in Fig. 1. The lung was sutured with two layers of continuous 2-0 atraumatic chromic catgut. When the upper lobe was incised, a large cavity with a shaggy purulent lining was demonstrated. The patient's postoperative course was not unusual except for the necessity of performing a 5-rib posterolateral thoracoplasty to obliterate an uninfected residual pleural air space. The sputum following resection became noninfectious. Vital capacity on Jan. 24, 1958, was 2,100 c.c. total and 1,500 c.c. in 3 seconds.

DISCUSSION

Ideally, surgery in patients with pulmonary insufficiency should remove tuberculous disease without sacrificing any functioning lung. Obviously no procedure can completely accomplish this; therefore, treatment of these patients requires various compromises. Occasionally, combinations of procedures must be used, such as segmental resection for a large rigid cavity and Monaldi cavernostomy for a smaller cavity which cannot be resected locally (Case 2), or lobectomy for extensive active disease involving a whole lobe, and local resection for a "healed" smooth-walled cavity in another lobe (Case 3).

Experience has shown that if cavitary disease can be excised, or otherwise obliterated, the remaining noncavitary disease is often well tolerated. Other factors being equal, there is an approximate quantitative relationship between the amount of disease and its effects upon the prognosis of the tuberculosis. However, the importance of residual disease varies with the bacteriologic state of the pulmonary tissue and the type of antituberculous drug therapy. The amount of disease is not very important when the lung has been rendered negative for culturable tubercle bacilli, a result which can be attained in the great majority of patients receiving long-term combined therapy with streptomycin, para-aminosalicylic acid, or isoniazid. The influence of residual disease upon prognosis is somewhat more important when culturable tubercle bacilli are present in the lung or sputum and long-term combined antituberculous drug therapy is administered postoperatively. The influence of residual disease is greatest in patients with infectious disease who receive single or short-term combined antituberculous drug therapy postoperatively.

From the functional point of view, percutaneous Monaldi cavernostomy is least disturbing to the patient. Open thoracotomy with concomitant tube cavernostomy or local resection of cavitary disease may be followed by little permanent decrease in ventilation. However, there is an early, often severe, decrease in ventilation which may not be tolerated well by a patient with severe pulmonary insufficiency. This early decrease in ventilatory capacity

does not occur following plombage thoracoplasty and, for this reason, plombage thoracoplasty is well tolerated by severely ill patients, provided a minimal amount of functional lung is collapsed.

Following thoracotomy it may be necessary to perform a tracheotomy to tide the patient over the period of early depression of ventilatory capacity. By this means pulmonary dead space is decreased and tracheobronchial secretions can be aspirated. We have not found it necessary to employ mechanical respirators or assistors to date. After the Monaldi procedure, patients with poor ventilatory capacity usually find that they can cough more effectively if they occlude the cavernostomy tube while coughing.

Of the three types of procedures discussed, plombage thoracoplasty seems to offer the poorest therapeutic results. However, the procedure does seem to offer some degree of palliation by reducing the amount of sputum and fever in many patients who do not achieve a noninfectious state. An advantage of this procedure, shared with percutaneous Monaldi cavernostomy, is that it can be performed with relatively little risk in the absence of concomitant antituberculous drug therapy. If multiple antituberculous drug therapy is available, one can expect much better therapeutic results with local cavitary resection and/or tube cavernostomy.

SUMMARY

The surgical treatment of pulmonary tuberculosis in patients with pulmonary insufficiency requires that as much functional lung as possible be preserved. Three procedures meet these functional requirements: plombage thoracoplasty, local excision of cavitary disease, and Monaldi cavernostomy. These may be employed separately or in combination. Important factors which influence therapeutic results are the presence of bacilli, antituberculous drug therapy, elimination of cavitary disease, and the amount of residual disease. In our experience, resection of cavitary disease and Monaldi cavernostomy have generally been more effective therapeutically than plombage thoracoplasty. When antituberculous therapy is not available, open thoracotomy should not be performed.

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POSTPNEUMONECTOMY OLEOTHORAX

Karl P. Klassen, M.D., and Neil C. Andrews, M.D., Columbus, Ohio

THE POSTPNEUMONECTOMY pleural space presents a definite problem in the management of patients having undergone pulmonary resection for congenital, infectious, traumatic, and neoplastic diseases. Because of the rigidity of the rib cage and instability of the mediastinum and diaphragm, it was generally assumed during the early days of pulmonary resection that with absorption of air and organization of the hemothorax, mediastinal shift to the side of resection would result in undesirable overdistention of the remaining lung. Experimental proof was brought forth that in growing, experimental animals[1, 2] such overdistention did not lead to impairment of pulmonary function but did in adult dogs. Clinical investigation of patients having undergone pneumonectomy in childhood supported this finding.[3] On the basis of clinical investigation,[4-7] it appears that such overdistention of normal pulmonary tissue in the adult is fairly well tolerated. Severe pulmonary emphysema, residual inflammatory disease, and other factors may, however, lead to progressive difficulties in the remaining lung.[8, 9]

The fate of the pleural space following pulmonary resection is fairly well understood. With adequate closure of the bronchial stump and chest wall, the pleural space will accumulate various amounts of blood depending upon the degree of trauma and hemostasis during surgery and on the type and duration of postoperative tube drainage. With removal of the drainage tube and in the absence of bronchial leakage and infection the early absorption of air will lead to shift of the mediastinum and elevation of the diaphragm. The resultant high negative pleural pressure may temporarily increase the amount of serosanguineous transudate. However, eventually over a period of months the fluid is absorbed and the cellular element becomes organized into a contractile fibrothorax with narrowing of rib spaces, marked mediastinal shift, and elevation of the diaphragm. Such contraction of the hemithorax may be minimal following a left pneumonectomy or in patients with preoperative diminution of the thorax due to long-standing previous congenital or infectious disease of the lung and pleura, and will present no particular problem. Occasionally, however, particularly in adults following right pneumonectomy, a contracting fibrothorax may lead not only to overdistention of the remaining emphysematous lung but also to marked deviation of the upper mediastinal

From The Division of Thoracic Surgery, Department of Surgery, The Ohio State University Health Center.

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structures, interfering with the normal function of the superior vena cava, trachea, and esophagus. Elevation of the left diaphragm may lead to trapped gastric air syndrome and occasionally to cardiac irregularities.

The first pneumonectomy performed by Graham in 1933[10] for bronchogenic carcinoma was combined with a thoracoplasty for obliteration of the pleural space. Since that time numerous laboratory and clinical studies have been presented in an attempt to solve the problem of the postpneumonectomy space. The consensus appears to be that overdistention of an emphysematous lung will further decrease its function, that severe mediastinal shift is undesirable, and that late infection may occur in the residual space.

Thoracoplasty performed concomitantly with the primary resection[11-13] or as a later separate procedure[14, 15] is used extensively at the present time; however, it is associated with definite disadvantages. Prolongation of the operative time, increased surgical trauma, and subsequent increased operative and postoperative blood loss are important factors in the older age group in a concomitant thoracoplasty. Subsequent multiple rib resections carry the risk and expense of an additional operative procedure. The deformities of thoracoplasties are objectionable from a cosmetic standpoint, particularly in women of the younger age group.

To overcome the objections of thoracoplasty, various forms of prostheses or space-filling devices have been tried. In 1949, Johnson[16] advocated the use of plastic spheres introduced into the pleural space as a form of plombage. This prosthesis has been used extensively for extrapleural plombage as well as in the postresection pleural space. Although the initial results appeared satisfactory,[17] a few later reports indicated difficulties with this material.[18] Ivalon sponge shaped to fit the pleural space was suggested by Grindley and Waugh[19] and subsequently used by others[20,21] apparently with good results, although late reports again indicate that difficulties were encountered in the presence of pleural space infection.[15, 22]

In 1951, we[23] reported our experience with sterile olive oil used as a prosthesis in 20 patients following pneumonectomy. Over a period of many years olive oil had been used extensively for the maintenance of pulmonary collapse in tuberculosis. Difficulties encountered with its use were numerous and stemmed apparently from its application in patients with pleural infection and in the presence of bronchial fistulas. The oil itself appeared to be well tolerated and did not lead to tissue reaction such as was produced by paraffin oil.

Since 1950, oleothorax has been used in our clinic as a postpneumonectomy prosthesis in 123 additional cases and a follow-up report dealing with our experience appears indicated.

PROCEDURE FOR THE ESTABLISHMENT OF OLEOTHORAX

Immediately following pneumonectomy, intercostal underwater-seal drainage is instituted and continued for 24 to 48 hours for the removal of accumulated blood and for the maintenance of normal intrathoracic pressure.

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Antibiotics are instilled into the pleural space on removal of the drainage tube and again just prior to discharge of the patient from the hospital, at which time the pleural pressure is neutralized.

The decision to establish an oleothorax is made during the postoperative period and depends upon preoperative pulmonary function, the condition of the remaining lung, the size of the pleural space, as well as on the operative findings and postoperative complications. Patients with previous contractile disease of the involved hemithorax and those with a small left pleural space and normal right lung usually show very little mediastinal shift and are not considered for oleothorax. Patients with known tuberculous pleural infection and with bronchial or cutaneous fistulas due to tuberculosis are treated by thoracoplasty. Patients with large residual pleural space, with emphysema or residual infection in the remaining lung and without evidence of pleural infection or bronchial fistula 4 weeks postoperatively are considered good candidates for the establishment of oleothorax.

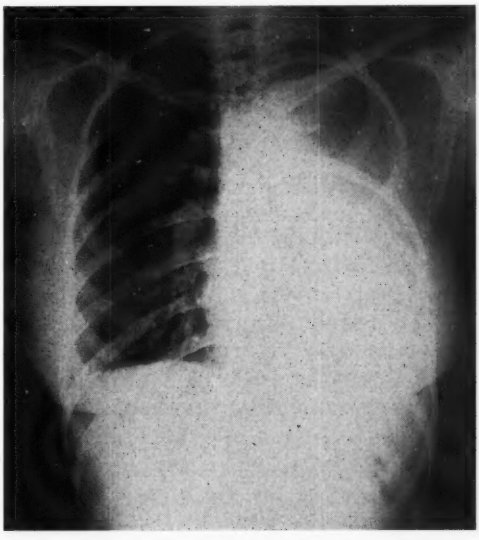

Fig. 1.—Roentgenogram showing excellent position of mediastinum 8 years following left pneumonectomy for tuberculosis and institution of oleothorax.

On re-admission to the hospital 4 to 5 weeks postoperatively, thoracentesis is performed using a No. 13 needle inserted through the seventh intercostal space in the midaxillary line. Following aspiration of the serosanguineous fluid, the patient is placed on the contralateral side and a second large needle is inserted for a distance of 2 cm. into the pleural space, one interspace above the first needle. This serves as an air vent. Sterile olive oil containing 1 Gm. of streptomycin and 300,000 units of penicillin per 500 c.c. is instilled into the pleural space through the first needle, using a 50 c.c. syringe. With the appearance of olive oil in the air vent needle, the instillation of oil is discontinued and both needles withdrawn. The amount of oil required for the

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establishment of the oleothorax depends on the size of the hemithorax and has varied in our patients from 300 to 2,700 c.c., with an average of 880 c.c. in the 149 patients. Immediately following the injection of oil, fluoroscopy is performed to determine the position of the mediastinum. There is usually a small cap of air in the apex of the pleural space containing an estimated 150 c.c. of air which becomes absorbed over a period of several weeks. When performed properly, the instillation of the oil produced very little discomfort and the patient is discharged from the hospital 24 hours later.

The oil used in these patients was commercial olive oil sterilized by dry heat for 3 hours at 160° C. and allowed to cool to room temperature. Bacteriologic study of samples of oil prepared by this method has shown this to be adequate for sterilization.

All patients return for regular postoperative visits and roentgenograms are taken at yearly intervals. Absorption of the oil does not occur and the mediastinum is maintained in its original position (Fig. 1). No attempt is made to evaluate the pressure within the pleural space unless the patient develops symptoms suggesting infection or increased amount of fluid. On several occasions samples have been taken from the oleothorax, which, however, show clear white oil and no evidence of emulsification in the absence of infection. The pressure in the lower thorax is slightly positive with the patient in the erect position, with a negative pressure while the patient is recumbent.

RESULTS

Oleothorax was established in 149 of 313 patients undergoing pneumonectomy for various conditions (Table I). The majority of resections were performed for bronchogenic carcinoma and in more than half of them oleothorax was utilized as a pleural prosthesis. During the 10-year period of this study, thoracoplasty was not used concomitantly with or subsequent to resection for bronchogenic carcinoma except in 1 patient who developed an empyema with a cutaneous sinus following the establishment of oleothorax. Sixteen patients died within a 30-day period following resection while in an equal number extensive mediastinal and pleural involvement indicated a short life expectancy contraindicating the use of oleothorax. Among the above patients were 8 with bronchial fistulas. In 2 patients, an early pyogenic empyema developed which, after successful treatment with antibiotics, resulted in a fibrothorax with obliteration of the pleural space. Fluid could not be aspirated in 2 patients because of loculation, while 2 patients failed to return for the oleothorax. In 65 patients, oleothorax was not considered necessary because of excellent function of the remaining lung, good position of the mediastinum in the postoperative period, and a small fluid-filled pleural space. The majority of these were on the left side.

There were 6 patients in this group who developed difficulties following instillation of the olive oil. An immediate acute empyema resulted in 2 patients within 48 hours of the instillation of oil. Following aspiration of the oil and intensive pleural and systemic antibiotic therapy the space became

TABLE I. OLEOTHORAX FOLLOWING PNEUMONECTOMY, 1948-1958

DIAGNOSIS	NUMBER OF PNEUMONECTOMIES	OLEOTHORAX ESTABLISHED	COMPLICATIONS	
			EMPYEMA	FISTULA
Bronchogenic carcinoma	225	122	3	3*
Tuberculosis	70	14	1*	
Bronchiectasis	13	8		
Adenoma	2	2		
Chronic pneumonitis	2	2		
Cystic disease	1	1		
Totals	313	149	4	3

*Due to primary disease.

sterile over a period of several weeks. The oleothorax was re-established in 1, while a fibrothorax developed in the second patient. In both of these patients, subsequent investigation revealed that a portion of the olive oil used had not been sterilized. An empyema developed in 1 patient 2 weeks following the oleothorax; however, it responded to pleural antibiotic instillation without removal of the oil. In 2 patients, late empyema developed following formation of a bronchial fistula found at autopsy to be due to residual carcinoma of the bronchial stump. In one of these patients there was also present an esophageal fistula due to carcinoma. A cutaneous sinus at the site of tube drainage developed in 1 patient with the loss of the oil and formation of an empyema treated subsequently by thoracoplasty.

Autopsies were performed on several patients with oleothorax of several years' duration who had died of recurrence of the bronchogenic carcinoma with extensive metastasis. The pleural space was found to contain a clear oil of approximately the amount instilled previously. The pleural surface was smooth and glistening, and microscopic sections showed a fibrous membrane containing oil spaces and very little inflammatory reaction (Fig. 2).

At the present time, there are 75 patients alive with oleothorax who have had resection for bronchogenic carcinoma. The longest survival is 10 years (Fig. 3). Forty-seven patients died at various intervals, following pneumonectomy and oleothorax, of progression of their bronchogenic carcinoma.

Pneumonectomy was performed in 70 patients with tuberculosis for destroyed lung, extensive excavation, bronchiectasis, bronchostenosis, and thoracoplasty failures. Tuberculous empyema associated with bronchial and cutaneous fistulas was present in a number of these patients. Oleothorax was established in only 13 patients who had no evidence of tuberculous pleural or bronchial disease. The oleothorax in these patients has been well tolerated. In 1 patient, an oleothorax was established in the presence of frank postresection tuberculous empyema in 1945. The patient did well and aspiration of a sample of oil in 1952 showed this to be clean and sterile on culture. The patient was lost to our observation, however, and died 5 years later of what was reported as a subphrenic abscess and tuberculous empyema. Detailed studies on this patient are not available at the present time.

In some of the patients with pulmonary tuberculosis, thoracoplasty had been performed prior to pneumonectomy and in others the disease process had resulted in such marked contraction of the chest wall and elevation of

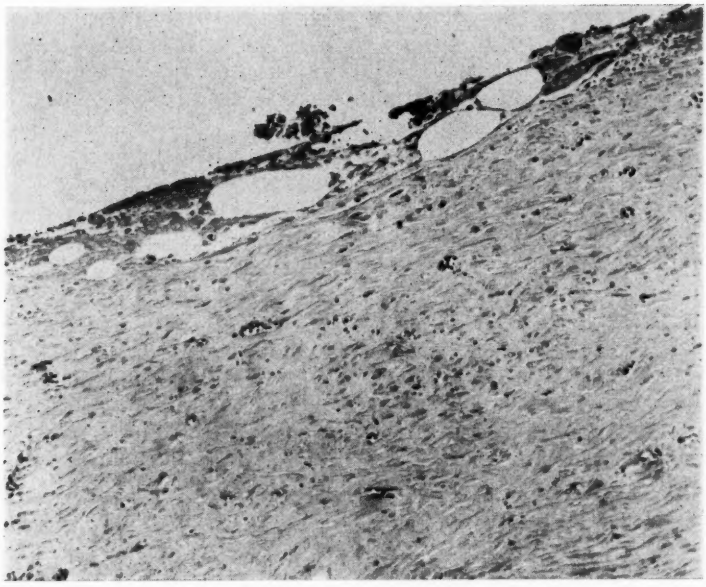

Fig. 2.—Photomicrograph of parietal pleura of a patient who died of bronchogenic carcinoma 1 year following pneumonectomy and establishment of oleothorax. Oil-containing spaces are shown as well as clumps of malignant cells on the surface. The underlying fibrous membrane shows little inflammatory reaction.

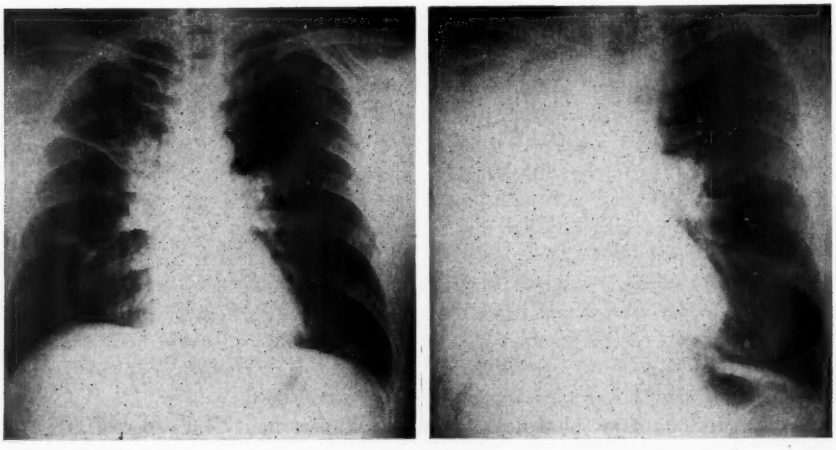

Fig. 3.—Roentgenogram of patient prior to pneumonectomy for bronchogenic carcinoma of right upper lobe in 1949 and present film showing oleothorax with minimal mediastinal shift.

the diaphragm that a space-filling prosthesis was unnecessary. In many of the patients with this disease, thoracoplasty was used to obliterate the postpneumonectomy space because of involvement of the pleura or transected bronchus.

In the patients with bronchiectasis involving an entire lung and necessitating pneumonectomy, 5 patients had a markedly contracted thorax resulting in a small postpneumonectomy space. In the remaining 8 patients, oleothorax was established and maintained without difficulty. In 2 patients with adenomas involving the main bronchus and regional lymph nodes requiring a pneumonectomy, oleothorax was established for cosmetic reasons, both patients being women in the middle age group. Two patients with chronic pneumonitis of unknown etiology had oleothorax established, while in 1 patient with congenital cystic disease of the lung there was no associated contraction of the hemithorax on the right side. A large pleural space remained, requiring the instillation of 2,500 c.c. of oil.

Since thoracoplasty has not been used routinely in our clinic following pneumonectomy for bronchogenic carcinoma, no data are available in determining the possible benefits of oleothorax over thoracoplasty in this disease, as far as function of the remaining lung is concerned. In a series of 11 patients, pre- and postoperative pulmonary function studies indicated an average loss of 30 per cent in the maximum breathing capacity. However, since the preoperative function of the removed lung varied from normal to complete absence of function, such comparative studies are of little value. It has been our clinical impression that patients with oleothorax, particularly in the presence of extensive emphysematous changes in the remaining lung, have done quite well. In patients who have developed pleural and distant metastases following oleothorax, accumulation of fluid in the pleural space has been no problem. It appears that the presence of oil may inhibit the effusion secondary to pleural carcinoma involvement. In 1 patient with extensive carcinomatosis of the pleura found at pneumonectomy, radioactive gold was used on two separate occasions prior to the instillation of oil. This patient lived without evidence of reaccumulation of fluid or mediastinal shift for 1 year and died of distant metastasis.

DISCUSSION

Oleothorax as used in our clinic over a period of 10 years in patients undergoing pneumonectomy has proved of definite value in the control of the postresectional space. The oleothorax can be established with ease and, when used with proper care and for definite indications, is well tolerated. Difficulties were encountered only in instances of improper application, such as its use in patients with infection of the pleural space, in the presence of bronchial disease leading to fistula formation, or inadequate sterilization of the olive oil. Once the oleothorax has been established it requires no additional attention, and patients followed for periods up to 10 years have had no late

complications because of the presence of the oil. The mediastinum has been maintained in its original position and no thoracic deformity has resulted.

We are continuing the use of oleothorax in patients presenting a problem in the control of a large pleural postpneumonectomy space. Overdistention of the remaining lung, undesirable shift of the mediastinum, and elevation of the diaphragm is prevented by the application of this prosthesis without additional surgery and without thoracic deformity. Oleothorax should not be used in the presence of pleural infection, actual or potential bronchial and cutaneous fistulas, or in patients with residual carcinoma of the bronchial stump. In patients with prepneumonectomy contracted thorax, those with previous thoracoplasty, and in patients with small residual fluid-filled space and good position of the remaining lung, a slight shift of the mediastinum is well tolerated and an oleothorax is not necessary.

SUMMARY

1. Oleothorax was applied as a postpneumonectomy pleural space prosthesis in 149 patients.

2. When applied under proper conditions, sterile olive oil was well tolerated in all patients for periods up to 10 years.

3. Infection of the oleothorax occurred in 7 patients. In 4 of these the complication was secondary to the original disease, while in 2, and possibly 3, improper sterilization of the oil resulted in an immediate empyema.

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ESOPHAGOPERICARDIAL FISTULA OF BENIGN ORIGIN

Sam E. Stephenson, Jr., M.D., Guy Maness, M.D., and
H. William Scott, Jr., M.D., Nashville, Tenn.

HYDROPNEUMOPERICARDIUM is a rare manifestation of disease. Shackelford,[1] in 1931, made a review of this entity and discussed the findings in 77 cases. Our attention was recently directed to the occurrence of hydropneumopericardium as a manifestation of benign esophagopericardial fistula. The development of such a fistula in an infant and the clinical problem which resulted seem worthy of reporting.

CASE REPORT

T. K. (V. U. H. #248643), an 11-month-old white male infant, was referred to the Vanderbilt University Hospital by his local physician for treatment of whooping cough. Past history from the mother revealed that the patient had enjoyed good health with normal growth and development until 5 weeks prior to admission when he developed fever and cough. This gradually developed into a paroxysmal cough which impressed the mother as being similar to the paroxysms of an older brother who had been diagnosed as having "whooping cough" 3 weeks previously. The patient also had episodes of vomiting with the paroxysms. Temperature at that time was 102° F., rectally, and little improvement was noted for the next few days. The patient had a generalized convulsive seizure 10 days prior to admission and was then examined by a local physician who made the diagnosis of pertussis and gave three injections of hyperimmune serum. Five days later the child was admitted to another hospital for treatment of progressive respiratory difficulty, cyanosis, and continuing fever. He was treated with oxygen, humidified air, and daily injections of antibiotics with a prompt fall in the fever to a normal range. His appetite improved and cough lessened but progressive respiratory difficulty continued. He was referred to the Vanderbilt University Hospital for further evaluation and treatment.

On admission the patient appeared acutely ill. Rectal temperature was 100.4° F., pulse 140 per minute, and respiratory rate 40 per minute. There was no cyanosis and peripheral veins were not dilated. Both lung fields were resonant with a few scattered harsh râles present bilaterally. The heart was normal, with no adventitious sounds. The liver was palpable one fingerbreadth below the right costal margin and the tip of the spleen was palpable. Blood pressure was recorded as 100/60 mm. Hg. There were no other significant findings.

Laboratory studies revealed that the urine was clear microscopically but contained two plus protein. Hemoglobin was 7.5 Gm. per 100 c.c. and the white blood count was 36,500 per cubic millimeter with 77 per cent neutrophils. Histoplasmin and tuberculosis skin tests were negative. Chemical determinations of the blood revealed carbon dioxide combining power 22.5 mEq./L., chloride 94.8 mEq./L., sodium 120 mEq./L., potassium 5.3 mEq./L., nonprotein nitrogen 24 mg. per cent, and serum protein 4.6 Gm. per cent with albumin-globulin ratio 2.7/1.9.

From the Department of Surgery, Vanderbilt University School of Medicine.
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Roentgenograms of the chest were interpreted as follows (Fig. 1): "Films show an open safety pin undoubtedly lying in the esophagus with its point directed forward and upward. The point distinctly lies within the cardiac silhouette. There are also scattered densities throughout both lung fields suggesting the presence of considerable pneumonitis. There is broadening and mottling of the mediastinal shadow, possibly representing a mediastinitis."

The patient was placed in a Batson box and humidified oxygen was administered. Intravenous fluids were started and 50 c.c. of whole blood was given. Eight hours after admission esophagoscopy was carried out (G. M.) and a rusty open safety pin was removed by advancing the foreign body into the stomach, rotating, and then extracting the pin. No definite perforation could be demonstrated at that time. The patient tolerated the procedure well and after intradermal testing was given tetanus antitoxin.

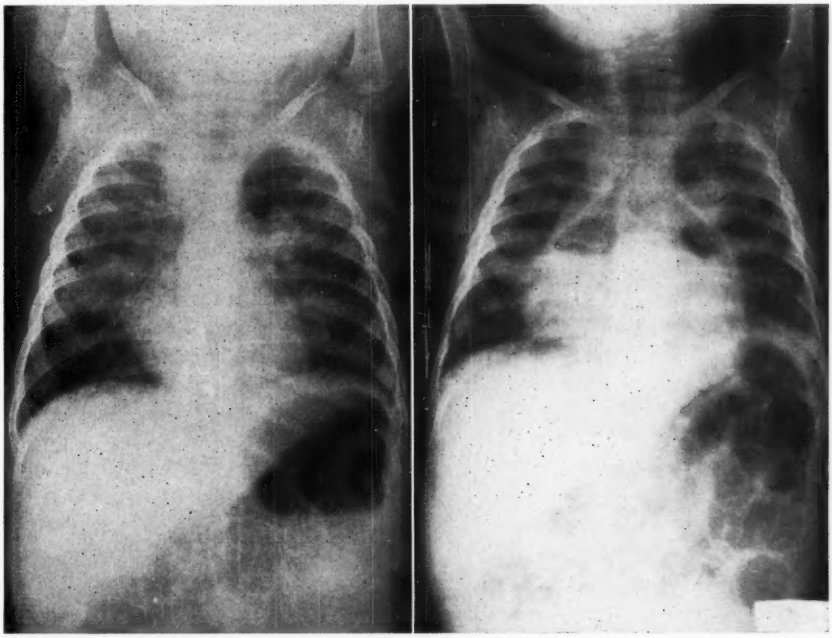

Fig. 1. Fig. 2.

Fig. 1.—Roentgenogram of the chest obtained on admission to the hospital showing open safety pin.

Fig. 2.—Roentgenogram of the chest obtained on the fifth hospital day showing marked increase in the size of the cardiac shadow, air-fluid level in the pericardial sac, and bilateral bronchopneumonia.

Cultures, reported on the second hospital day, grew out *Pseudomonas aeruginosa* from a throat swab and coliform organisms from blood. These organisms were sensitive to streptomycin and chloramphenicol and these drugs were started. Oral feedings were begun 2 days after extraction of the safety pin. The child made little improvement on treatment but no great change was noted until the fifth hospital day when he suddenly appeared moribund. Examination at this time revealed periorbital edema in spite of previous fluid restriction. The liver and spleen had each increased in size and some peripheral edema was noted. The heart sounds were muffled but no *bruit de moulin* was audible. An immediate

chest roentgenogram revealed a marked increase in the size of the cardiac silhouette with an air-fluid level in the pericardium (Fig. 2). Venous pressure at this time was 340 mm. of saline. The electrocardiogram revealed low voltage and the neck veins were visibly distended.

The diagnosis of esophagopericardial fistula with cardiac tamponade was made and operation was carried out immediately. Using 0.5 per cent lidocaine hydrochloride infiltration anesthesia, a segment of the fifth costal cartilage was excised. The pericardium was exposed and incised releasing 100 to 150 c.c. of serosanguineous fluid with the distinct odor of Meade's 367, the infant's oral nutrient. Immediately on release of the air and fluid, the infant's color improved. He began to cry vigorously and to struggle on the table. The pericardium was sutured to the skin edges to ensure proper drainage by marsupialization.

Fig. 3.—Esophagogram obtained by injecting Iodochloral on the sixth postoperative day which reveals a normal-appearing esophagus with no evidence of a functioning fistula.

The early postoperative period showed a remarkable improvement. The child remained alert and the temperature fell toward normal levels. The enlargement of the liver and spleen and the peripheral edema regressed. However, slight edema persisted and after 6 days a low-grade fever was still present. At this time the patient was digitalized with little improvement. Drainage from the pericardiostomy gradually ceased. Methylene blue was given by mouth as was Iodochloral without demonstrating a functioning fistula either visually or fluoroscopically (Fig. 3). Oral feedings were then started in small amounts and the patient maintained a slow improvement until the night of the tenth postoperative day when he again suddenly developed marked respiratory difficulty, air hunger, and

abdominal distention. Roentgenogram of the chest revealed a normal sized heart but bilateral pleural effusion and a dense scattered bilateral pulmonary infiltrate. The patient deteriorated rapidly and died on the eleventh postoperative day.

Pertinent findings at necropsy were limited to the thoracic cavity. Approximately 10 c.c. of clear fluid was present in the right pleural cavity and the left pleural cavity was obliterated by adhesions. The mediastinal tissues were edematous and inflamed. Adhesions were present between the visceral and parietal pericardium. Two and one-half centimeters above the esophagogastric junction on the anterior surface of the esophagus was a 1 mm. perforation through which a probe could be passed. The probe emerged through the parietal pericardium adjacent and posterior to the junction of the right auricle and inferior vena cava. On opening the heart there was a mural thrombus on the posterior aspect of the right ventricular wall. The thrombus was 0.5 by 0.5 cm. in size and on cut section its central portion was noted to be purulent.

The right lower lobe contained multiple elevated, hard, bluish nodules in the subpleural area. On cut section these areas were typical of multiple pulmonary infarcts and, in fact, some areas of infarction were undergoing suppuration. Microscopic sections supported the fact that these were mycotic emboli. Multiple areas of infarction were also scattered throughout the remainder of the right and left lungs. Cultures taken at the time of autopsy grew out *Pseudomonas aeruginosa* from the tracheobronchial tree and *Candida albicans* from the mural thrombus.

COMMENT

Hydropneumopericardium has been recognized as a clinical entity for over a hundred years. Shackelford[1] credited the first documented case to Bricheteau,[2] in 1844. James,[3] in reviewing the same malady in 1904, found 38 cases of hydropneumopericardium and of these only 6 represented an esophagopericardial fistula of benign origin. According to James, Buist[4] described the first esophagopericardial fistula in 1838. We have been able to find 6 additional cases reported since James's review in 1904. The present case is apparently the thirteenth case to be reported (Table I). A recent article by McDaniel[5] referred to 11 cases of fistula secondary to benign conditions. However, the second case of Abbott[6] and that of Drouet[7] were omitted and the case of Chamber[3] was referred to as a benign ulcer when in fact it was secondary to an esophageal carcinoma.

The cases of esophagopericardial fistula arising secondary to neoplastic disease have not been included in Table I. We feel that an ulcerated, perforated neoplasm of the esophagus is probably beyond the bounds of curative resective surgery. The appalling fact is that all 13 patients suffering from benign esophagopericardial fistula have died. The diagnosis was made clinically in 8 cases, by necropsy in 4, and, in 1, at the time of surgical intervention. Only 4 of the 8 cases diagnosed clinically were subjected to surgery with 4 postoperative deaths 22 hours, 3 days, 11 days, and 14 days, respectively. The over-all mortality in the series is 100 per cent. This is a discouraging record in a benign condition which should be amenable to prompt surgical intervention and saving of the patient's life. The death of our patient was due actually to a complication of the initial myocardial perforation rather than the pericardial opening. All of the evidence before death indicated functional closure of the esophagopericardial fistula.

TABLE I. COLLECTED CASES OF ESOPHAGOPERICARDIAL FISTULA ARISING SECONDARY TO BENIGN CONDITIONS

AUTHOR	YEAR	AGE	CAUSE	PHYSICAL SIGNS	DIAGNOSIS	OUTCOME	AUTOPSY
1. Buist[4]	1838		Laceration esophagus from false teeth	None recognized	Autopsy	Died	Yes
2. Trotter[9]	1851	25 yr.	Perforated benign ulcer of esophagus	None recognized	Autopsy	Died	Yes
3. Walske[10]	1873		Perforation of esophagus from swallowing sword	Tympanitic precordium	Clinical	Died	Yes
4. Meigs[11]	1875		Perforated benign ulcer	Succussion splash	Clinical	Died	Yes
5. Huber[12]	1903		Erosion from lymph node	Tympanitic precordium	Clinical	Died	Yes
6. James[3]	1904		Perforated esophagus from ingested bone	Succussion splash, shifting dullness	Clinical	Died; 1 day postop.	Yes
7. Imperatori[13]	1928	13 mo.	Foreign body (safety pin) perforation	Bronchopneumonia	X-ray	Died	Yes
8. Abbott[6]	1945	6 days	Fistula following cauterization of web	Bronchopneumonia	Autopsy	Died	Yes
9. Abbott[6]	1945	46 yr.	Pulsion diverticulum; postop. emphysema	Succussion splash	Clinical	Died; 14 days postop.	Yes
10. Massias and Nguyen[14]	1948		Foreign body	Succussion splash	Clinical	Died	Yes
11. Drouet et al.[7]	1955	52 yr.	TBC abscess of mediastinum	Perforated esophagus	At exploration	Died; 3 days postop.	No
12. McDaniel and Knepper[5]	1956	60 yr.	Unknown	Succussion splash	Clinical	Died	Yes
13. Authors	1958	11 mo.	Foreign body (safety pin)	Cardiac tamponade	Clinical	Died; 11 days postop.	Yes

The physical findings of hydropneumopericardium are classical. The succussion splash or *bruit de moulin* synchronous with cardiac systole occurs with no other known condition. Cardiac tamponade which presented in our patient[8] has also occurred in 3 additional cases. The routine use of the roentgenogram should permit an earlier diagnosis before the physical findings of cardiac tamponade have developed. The demonstration of an air-fluid level in the pericardium establishes the diagnosis without question.

The possibility of this condition as a complication of ingested foreign bodies must be kept in mind and early surgical intervention is mandatory if esophagopericardial fistula is to be treated successfully. The condition of the patient will by necessity dictate a direct or indirect surgical approach. There can be no question that the procedure of choice would be a closure of the fistula with adequate toilet and drainage of the pericardium but marsupialization of the pericardium in an acutely ill, moribund patient could be lifesaving.

SUMMARY

1. A case of benign esophagopericardial fistula secondary to an ingested foreign body is reported.

2. A review of the literature reveals that 12 other cases of benign esophagopericardial fistula have been reported in the last century.

3. The mortality of this condition has been 100 per cent.

4. Although the diagnosis has been made clinically in 8 cases, only 4 have been subjected to surgical intervention.

5. Awareness of the possibility of this condition as a complication of ingested foreign bodies by pediatricians, endoscopists, radiologists, and surgeons and prompt surgical intervention offer the only hope for improvement in the survival rate.

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AN INVESTIGATION OF CARDIAC ARREST PRODUCED BY INJECTION OF POTASSIUM CITRATE INTO THE CORONARY CIRCULATION

James A. Helmsworth, M.D., Ralph W. Shabetai, M.R.C.P., and Joseph Margolian, M.D., Cincinnati, Ohio

HEART-LUNG machines are now employed successfully in many centers and their use has permitted improvement in surgery for a number of different cardiac malformations. Optimum conditions for the correction of deformities within the heart will not be attained, however, until asystole can be induced. Although this is a radical concept, it is the conclusion of most investigators who have had experience with surgery in the open heart during perfusion of the body.

Melrose's preliminary communication on elective cardiac arrest induced by intra-aortic injection of potassium citrate solution[1] has been widely received. The majority of investigators in this field have tried the technique and it has been adopted for clinical use by several leading centers for cardiac surgery.[2, 3] Experience in our laboratory, however, aroused suspicion that this technique for asystole was the cause of serious myocardial damage. We therefore adopted this as an hypothesis and planned two series of experiments to test it. The present report summarizes the first series.

METHOD

Dogs of medium size were anesthetized with pentobarbital sodium given intravenously and ventilation was maintained through a large endotracheal tube. One hundred per cent oxygen was administered by a mechanical ventilator and soda lime was used for the absorption of carbon dioxide from the semiclosed system. The femoral artery and vein were cannulated for pressure measurements. A bilateral thoracotomy was made through the fourth intercostal spaces and the sternum was transected. In the groups of experiments in which the vena cavas were to be occluded, these vessels were isolated in the standard manner. The pericardium was opened widely in all animals and the aorta was dissected from the pulmonary trunk for a distance of 2 cm. above the origins of the coronary arteries. A plastic tube (6 mm., i.d., and 50 cm. long) was inserted into the left atrium via its appendage. The outer end of the tube was

From the Department of Surgery and Cardiology Laboratory, Department of Internal Medicine, College of Medicine, University of Cincinnati.

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passed through the wall of the left chest and supported at a level of 15 cm. below the left atrium. This tube provided the simplest system possible for rapid removal of aliquots from the left atrium.

The first group of 5 experiments comprised one control series. Two samples were withdrawn from the left atrial tube for determination of the serum potassium level immediately prior to the test conditions. No potassium citrate was injected but the vena cavas and aorta were occluded simultaneously, except in 1 experiment noted below. The pulmonary artery remained open as

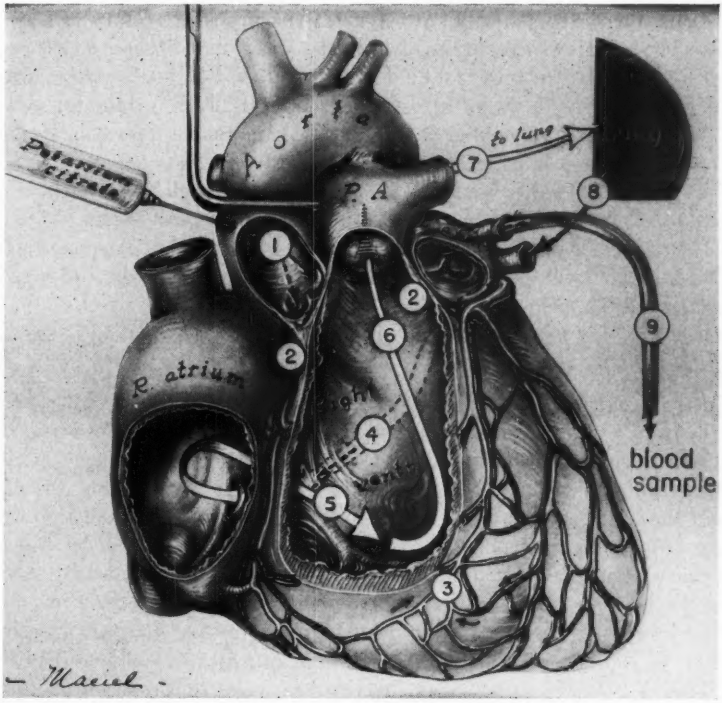

Fig. 1.—The level of aortic occlusion is illustrated as well as the site of potassium citrate injection and the system for collection of blood samples from the left atrium. The course of "isolated cardiac circulation" is shown by the continuous arrow through serially numbered locations. Emphasis is laid on the recirculation of blood from the coronary sinus through the lungs and back into the chambers of the left side of the heart.

it did in all of the other groups. Samples of blood were taken from the left atrium at intervals of 10 seconds during the 3 minutes of aortic and caval occlusion, and the concentration of serum potassium was determined in each sample. These 5 animals were allowed to recover and after approximately 30 minutes, were subjected to the experiment outlined for Group 3.

The second group of experiments included 10 animals. Two control samples were withdrawn from the left atrium and immediately after this potassium citrate solution (2 c.c. of 25 per cent solution with 18 c.c. of arterial blood)

was injected into the occluded aorta so as to perfuse the coronary arteries. The dose of potassium citrate was the amount required to arrest the heart. The vena cavas were not occluded in this series. Ten blood samples for serum potassium determinations were drained from the left atrium *after* cardiac arrest. The interval between samples was approximately 10 seconds.

The third group comprised 11 dogs in which potassium citrate in the same dilution was injected into the occluded aorta. Again, the amount injected was just enough to cause asystole. In this group, however, the vena cavas were occluded simultaneously with the aortic occlusion. Sampling from the left atrium was identical in technique to that of the previous group.

The last group, consisting of 4 animals, was an additional control series. The aorta and vena cavas were occluded and asystole was produced by injection of acetylcholine (100 mg. in 10 c.c. of physiologic saline) into the occluded aorta. Samples were taken from the left atrium using the same technique employed in the preceding groups.

Fig. 1 illustrates the course of the circulation through the heart and lungs and the site from which blood samples were drawn after occlusion of the aorta.

The analysis of serum samples for potassium content was completed without delay, using the Janke flame photometer. The variation in duplicate samples did not exceed 0.1 mEq./L.

RESULTS

In the groups of experiments in which potassium citrate was injected and in both groups of controls, the heart continued to contract effectively for 10 seconds or longer after the aorta was clamped. During this brief period of isolated cardiac circulation the effluent from the myocardium was forced through the lungs again by the right ventricle. This blood flowed into the left atrium and ventricle, was pumped out once more and forced by the aortic obstruction to re-enter the coronary circuit. This may be clarified by reference to Fig. 1 where an arrow connects the anatomic sites, labeled seriatim.

The levels of potassium observed in the first group of controls are given in Table I. A significant elevation of potassium contents was observed in only 2 dogs, 17 and 19. The former may illustrate chemical confirmation of a clinical impression. This animal had the aorta closed by accident 20 seconds prior to interruption of caval flow, causing the heart to become greatly distended. The tone of the myocardium never returned to normal and when, a short time later, the heart was arrested with potassium citrate, it continued to lose potassium as shown in Table III. We suspect that acute cardiac dilatation of this type results in cellular damage and this, as has been shown by Harris[4] is reflected in elevation of the potassium content of coronary venous blood. The remaining experiments in this control series indicate that, in a short period of combined aortic and caval occlusion, there is no significant change in the potassium content of blood collected from the left atrium.

In the second group of animals in which potassium citrate was injected into the occluded aorta, and the vena cavas were not occluded, a relatively large flow continued through the right heart until asystole developed. The results from

TABLE I. POTASSIUM CONCENTRATION IN SERIAL SAMPLES FROM LEFT ATRIUM DURING 3-MINUTE OCCLUSION OF VENA CAVAS AND AORTA WITHOUT INJECTION OF POTASSIUM CITRATE

DOG NO.	CONTROL LEVEL K IN LEFT ATRIAL BLOOD (mEq./L.)	PEAK LEVEL K IN LEFT ATRIAL SAMPLES (mEq./L.)
17	4.7	7.4
19	3.6	4.0
20	4.3	4.5
21	5.4	5.5
22	3.8	3.6

this group are listed in Table II. Most of the hearts contracted 14 to 25 times after the start of the potassium citrate injection. Blood withdrawn from the left atrium after asystole was induced showed peak levels of potassium in the range of 10 to 30 mEq./L. in the majority of animals. A comparison between the total dose of potassium administered and the total amount recovered in drainage from the left atrium must be made cautiously, because calculation of the latter value is subject to error of varying degree. It is certain, however, that in 2 of the group, Dogs 6 and 7, the potassium recovered from the left atrium was in excess of the dose administered. This, in the light of the work of Harris and Hamilton and their colleagues,[4, 5] may indicate myocardial damage.

TABLE II. POTASSIUM IN SERIAL SAMPLES FROM LEFT ATRIUM FOLLOWING AORTIC OCCLUSION AND ARREST WITH INJECTION OF POTASSIUM CITRATE (PULMONARY ARTERY AND VENA CAVAS NOT OCCLUDED)

DOG NO.	NO. HEARTBEATS FROM START OF INJECTION TO ARREST	CONTROL LEVEL K LEFT ATRIUM (mEq./L.)	PEAK LEVEL K LEFT ATRIUM (mEq./L.)	TOTAL DOSE K (mEq./L.)	TOTAL K RECOVERED (mEq./L.)
1	10	4.6	9.8	1.15	0.53
2	14	3.8	20.5	1.38	1.03
3	60	4.7	26.0	3.68	1.80
4	6	4.3	5.9	0.92	1.0
5	22	2.9	8.3	1.84	0.52
6	20	3.9	31.0	1.84	2.50
7	22	2.4	35.0	2.53	3.60
8	25	3.8	9.5	1.61	0.56
9	14	3.5	11.7	1.38	0.59
10	6	2.5	10.6	0.92	0.46

Table III summarizes data from Group 3, the animals with occlusion of the vena cavas and the aorta and injection of potassium citrate. In these experiments the only flow through the right heart was the volume from the coronary sinus. The conditions of this experiment consequently resembled closely the technique employed for potassium citrate asystole in clinical practice. The ventricles continued with 10 to 20 contractions in the majority of experiments after the start of the potassium citrate injection. The peak levels of potassium in left atrial samples drawn after arrest exceeded 30 mEq./L. in over half the animals. Experiments in 4 dogs, 11, 12, 18, and 19, demonstrated a notable excess of potassium in blood collected from the left atrium above the amount injected into the coronary circuit. Dog No. 17 is not grouped with these 4 because of the change noted in the control period and mentioned in discussion of Table I.

TABLE III. POTASSIUM IN SERIAL SAMPLES FROM LEFT ATRIUM FOLLOWING OCCLUSION OF VENA CAVAS AND AORTA AND ARREST WITH INJECTION OF POTASSIUM CITRATE (PULMONARY ARTERY NOT OCCLUDED)

DOG NO.	NO. HEARTBEATS FROM START OF INJECTION TO ARREST	CONTROL LEVEL K LEFT ATRIUM (mEq./L.)	PEAK LEVEL K LEFT ATRIUM (mEq./L.)	TOTAL DOSE K (mEq./L.)	TOTAL K RECOVERED (mEq./L.)
11	--	3.5	90.0	1.84	2.4
12	10	4.0	49.0	1.38	1.85
13	9	4.3	36.0	1.15	0.86
14	9	5.6	31.5	2.30	---
15	25	5.6	9.1	7.36	3.6
16	50	4.9	21.2	1.84	0.80
17	--	5.0	47.0	2.99	5.12
18	29	4.0	113.0	3.45	4.76
19	13	3.4	61.0	2.07	3.10
20	--	4.5	22.0	3.22	1.67
22	20	3.6	18.1	4.3	2.5

The highest levels of potassium for the individual experiments of Group 4 (aortic and vena caval occlusion and asystole produced by acetylcholine) are given in Table IV. The peak values of potassium were slightly higher than the control values. This change was in the range observed in the first control series where left atrial samples were taken during aortic and caval occlusion without asystole.

TABLE IV. POTASSIUM IN SERIAL SAMPLES FROM LEFT ATRIUM FOLLOWING OCCLUSION OF VENA CAVAS AND AORTA AND ARREST WITH INJECTION OF ACETYLCHOLINE

DOG NO.	CONTROL LEVEL K LEFT ATRIUM (mEq./L.)	PEAK LEVEL K LEFT ATRIUM (mEq./L.)
23	3.9	4.2
24	3.0	3.5
25	4.5	4.8
26	3.7	3.5

DISCUSSION

This study is concerned primarily with the potassium content of blood in the left heart or entering it from the pulmonary circuit after asystole induced by the injection of potassium citrate into the coronary circulation. The relatively concentrated injectate perfuses the coronary system but ventricular contractions continue long enough to force the coronary sinus effluent back into the pulmonary circulation. The method of this experiment permits sampling of blood draining from the pulmonary venous system into the left atrium. Experiments of Groups 1 and 4 indicate that during the short period of observation after occlusion of the aorta and vena cavas the potassium content of blood in the pulmonary vessels and left atrium rose 0.5 mEq./L. or less. Experiments of Groups 2 and 3 revealed a relatively high concentration of potassium to which the left heart is exposed when asystole is induced by the Melrose method. We suspect that these high levels of blood potassium may be correlated with complications encountered in the left ventricle after use of

this technique. In a significant number of the dogs in Groups 2 and 3, there was loss of potassium from the myocardium into the coronary venous blood and this strongly suggests that there was acute injury to the heart.

SUMMARY

1. Experiments were done in which the level of potassium was measured in blood samples drawn from the left atrium. The potassium rose very slightly in a simple control group in which asystole was not induced. A similar slight rise was observed in another control group in which asystole was produced by acetylcholine.

2. Two groups of animals were studied in which the heart was arrested by potassium citrate and blood samples were taken from the left atrium. High concentrations of potassium were found in blood samples from this chamber.

3. Some of the animals subjected to potassium citrate asystole lost additional amounts of potassium from the myocardium.

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THE LOCAL EFFECT OF POTASSIUM CITRATE SOLUTION IN ATRIAL POUCHES OF DOGS

James A. Helmsworth, M.D., Ralph W. Shabetai, M.R.C.P.(Edin.), John E. Albers, M.D., and Paul J. Wozencraft, M.D., Cincinnati, Ohio

THE MELROSE technique for cardiac arrest has been adopted with very little delay by several outstanding surgical centers.[1, 2, 3] When it is tried in the laboratory and the animal's life is maintained by total body perfusion, it appears to be entirely reliable for the induction and maintenance of asystole. However, the rate of long-term survival after cardiac arrest by potassium citrate during total perfusion in dogs is stated only infrequently, and may be relatively low.[4]

Our own experience with the method has caused us to suspect that myocardial injury may result from its use. An earlier series of experiments demonstrated that the left atrium and ventricle are often exposed to very high concentrations of potassium when the injection is made into the occluded aorta in the usual way.[5] It is possible that pooling of potassium-rich blood in the left heart chambers is related to the abnormal tonic type of contraction of the left ventricle that has occasionally been observed following arrest of the dog's heart with potassium.[6] We questioned whether the high concentration of potassium within the cardiac chambers could be harmful to the endocardium and subjacent muscle, and planned a simple experiment to explore this possibility. The present report summarizes the experiment, the second in a series of two planned to test the hypothesis that use of the Melrose technique is the cause of myocardial damage in dogs.

METHOD

Mongrel dogs were employed and only those with signs of distemper were considered unsuitable for the experiment. The methods for anesthesia and ventilation were the usual ones used in this laboratory and described in an earlier report.[5] The blood pressure was observed by means of a mercury manometer attached to the femoral artery. Both pleural spaces were opened through short incisions between the fourth and fifth ribs. The pericardium was opened through two incisions, each one parallel with and ventral to the

From the Department of Surgery, Cardiology Laboratory, Department of Medicine and Department of Pathology, College of Medicine, University of Cincinnati.

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phrenic nerve on the corresponding side. The atrial appendages were easily lifted into the pericardial incisions and small forceps with atraumatic blades were applied so as to occlude them at their bases as illustrated in Fig. 1. Occlusion of the atrial appendage on one side served as a control on the factor of trauma. The clamped appendage on the other side served as the experimental pouch. Blood was withdrawn from the isolated pouch with a small needle and replaced with a solution of potassium citrate. Leakage from the puncture site was prevented by a fine silk mattress suture.

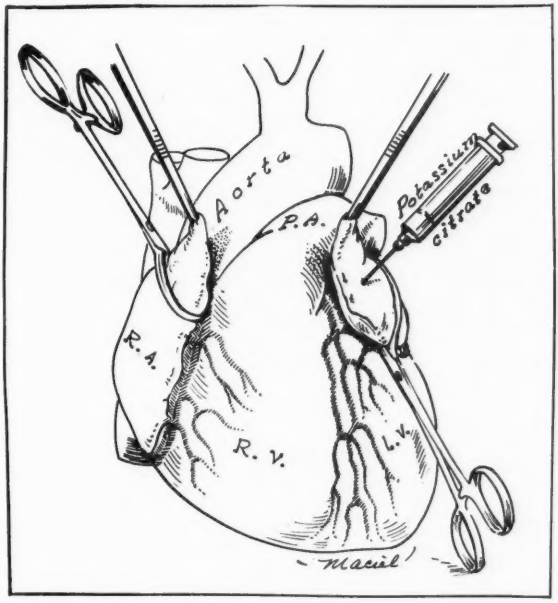

Fig. 1.—The appendage of each atrium was elevated and occluded at its base with an atraumatic clamp. In the experiment illustrated, the empty left appendage was filled with potassium citrate solution. The right appendage was subjected to the same surgical trauma and served as a control.

The 16 animals in the experiment were divided into two groups. The first included only 5 dogs and in these the experimental atrial pouch was filled with 25 per cent solution of potassium citrate. The volume required varied from 1.5 to 4.0 c.c. and overdistention was avoided. Thus, in this group, the total amount of potassium administered was similar to that employed clinically but the solution was much more concentrated since it was not mixed with blood.

The second group of 11 dogs received potassium citrate in a more dilute form. In a previous study we found that with the Melrose technique the concentration of potassium in blood recovered from the left atrium averaged 30 mEq./L.[5] In this group, therefore, the atrial pouch on the experimental side was filled with potassium citrate solution in concentration of 30 mEq./L.

The forceps remained in position for 30 minutes and then the appendages were released and allowed to retract into the pericardium. The potassium citrate was allowed to escape into the atrium at the conclusion of the first few experiments. This was invariably associated with serious arrythmias and, therefore, in all subsequent experiments, the chemical was aspirated from the appendage at the end of 30 minutes before removal of the atraumatic clamp. The appendages were removed later for microscopic examination and the pathologist (P. J. W.) was not informed which one was the experimental and which one was the control pouch. Animals that did not recover fully from the procedure were included in the study; the time interval between potassium instillation and death is given in Tables I and II. All survivors were sacrificed on the third day after the experiment.

RESULTS AND DISCUSSION

Table I summarizes the findings in the group of dogs injected with the more concentrated solution of potassium citrate. Four out of 5 showed myocardial necrosis in the experimental pouch and none in the control appendage. This change was present in every animal that survived 24 hours or longer after instillation of the chemical. It is shown in Fig. 2 which is a photomicrograph of the experimental pouch from Dog 401 in this series. Epicarditis and interstitial hemorrhage were the only changes observed in the appendages that served as controls. The characteristic histologic picture of the myocardium in control pouches is shown in Fig. 3.

TABLE I. RESULTS IN ANIMALS IN WHICH 25 PER CENT SOLUTION OF POTASSIUM CITRATE WAS INJECTED

DOG NO.	SURVIVAL (HR.)	ATRIAL POUCH WITH POTASSIUM CITRATE	CONTROL ATRIAL POUCH
389	72	Severe and extensive necrosis of myocardium	Normal except for area of acute epicarditis
401	24	Severe myocarditis with scattered areas of necrosis	Normal
403	72	Extensive myocardial necrosis with interstitial hemorrhage	Normal
405	1	Normal	Myocardium normal; extensive interstitial hemorrhage
407	40	Widespread myocarditis with areas of necrosis	Normal except for mild epicarditis

Table II lists the pathologic changes in the atrial pouches injected with the dilute solution of potassium citrate. Six dogs (416, 417, 420, 421, 423, 441) out of 11 in this group had necrosis in the experimental pouch whereas this change was not found in the control pouch of any animal in the series. Figs. 4 and 5 are photomicrographs of the experimental and control pouches, respectively, from Dog 441. In 2 additional dogs (412, 413) the inflammatory reaction in the epicardium, myocardium, and endocardium was more severe in the experimental pouch than in the control. Three dogs (426, 434, 435) showed changes in the control pouches as severe as those seen in the experimental side. It was difficult, if not impossible, to determine if epicardial reaction extended into the wall of a structure as thin as the atrial appendage but

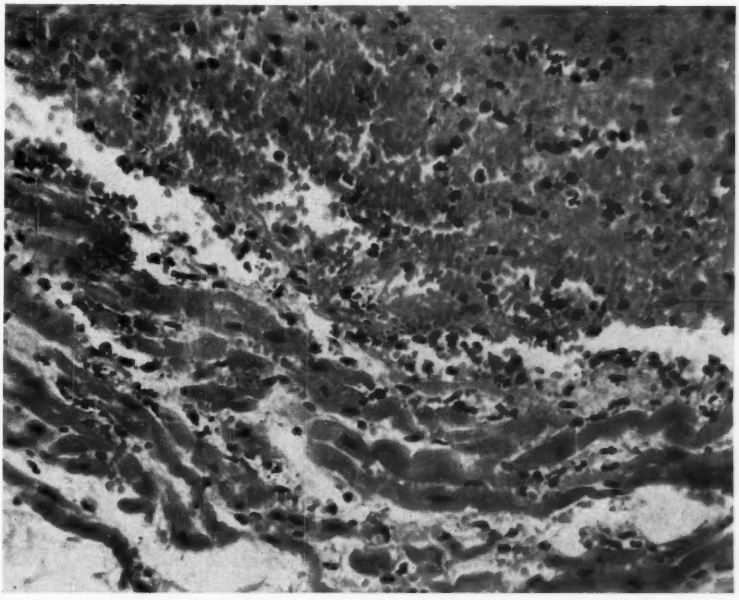

Fig. 2.—Photomicrograph from atrial pouch exposed to potassium citrate solution (25 per cent) and removed 24 hours later (Dog 401). There is severe myocarditis with areas of necrosis.

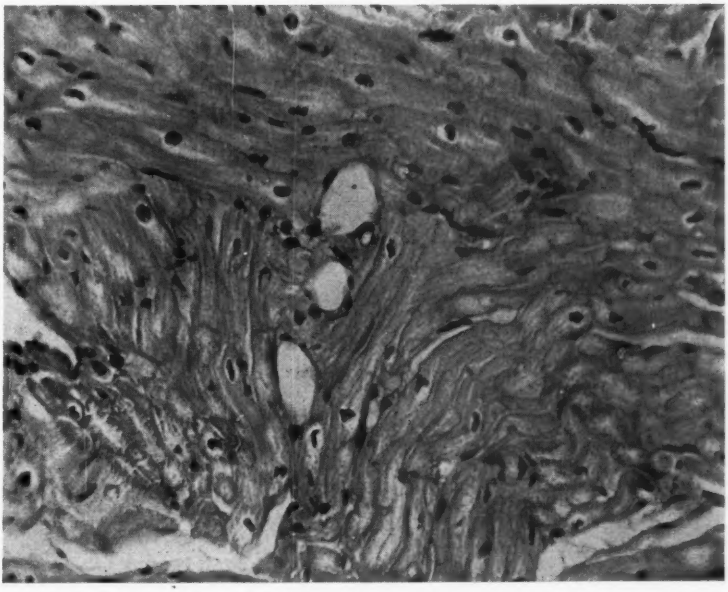

Fig. 3.—Photomicrograph from control atrial pouch removed 24 hours after experiment (Dog 401). The histologic picture is normal.

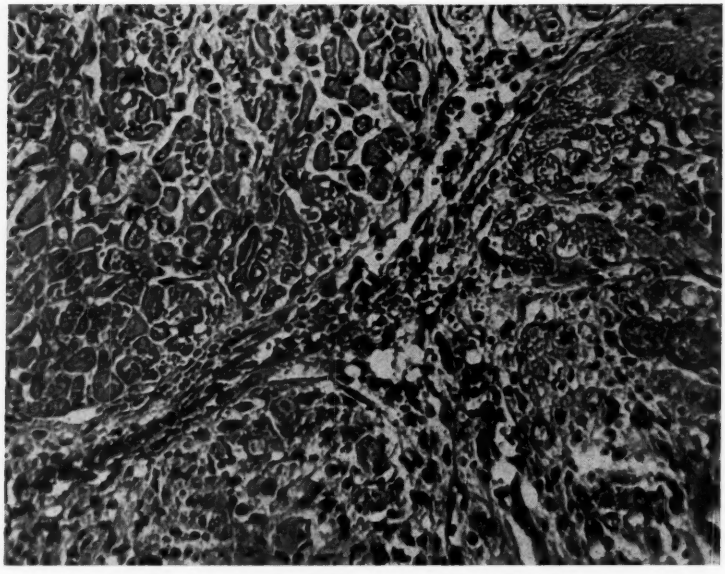

Fig. 4.—Photomicrograph from atrial pouch exposed to potassium citrate solution (30 mEq./L.) and removed 72 hours later (Dog 441). Widespread inflammation is shown and some necrosis of the myocardium.

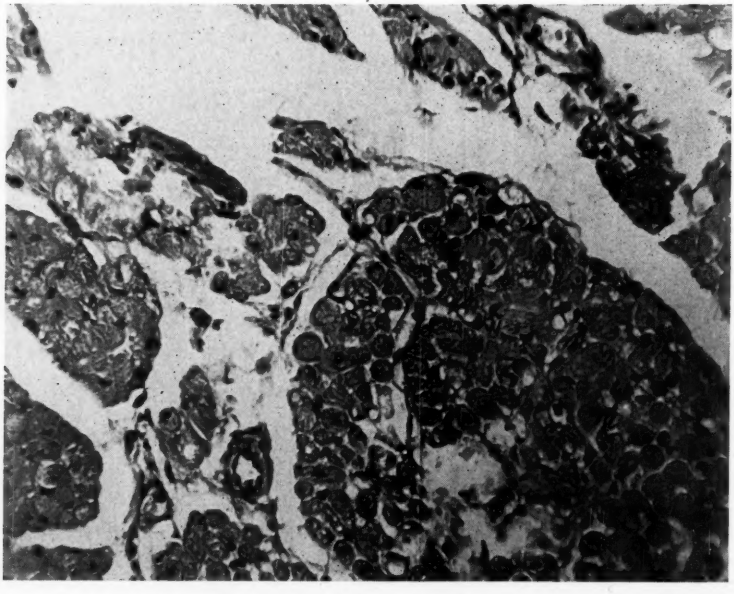

Fig. 5.—Photomicrograph from control atrial pouch removed 72 hours after experiment (Dog 441). There is slight epicarditis.

the changes were described as progressing this way in 3 experiments (423, 434, 435). Inward extension of epicardial reaction would be more likely to result from trauma and infection than from the chemical agent instilled into the endocardium but it was impossible to clarify this point by these experiments.

TABLE II. RESULTS IN ANIMALS IN WHICH DILUTE SOLUTION OF POTASSIUM CITRATE WAS INJECTED

DOG NO.	SURVIVAL (HR.)	ATRIAL POUCH WITH POTASSIUM CITRATE	CONTROL ATRIAL POUCH
412	48	Epicarditis and small focus of myocarditis and endocarditis	Epicarditis
413	72	Epicarditis and focal myocarditis and endocarditis	Epicarditis
416	48	Epicarditis and focus of myocardial necrosis	Epicarditis
417	24	Epicarditis and foci of myocardial necrosis	Epicarditis
420	24	Epicarditis; necrosis, hemorrhage and inflammation of myocardium	Epicarditis
421	24	Epicarditis with diffuse myocarditis and patchy necrosis	Epicarditis
423	72	Epicarditis; patchy endocarditis and myocardial necrosis	Epicarditis with some extension into myocardium
426	24	Epicarditis and focal myocarditis	Epicarditis and focal myocarditis
434	24	Epicarditis extending into myocardium	Epicarditis extending into myocardium
435	72	Severe patchy epicarditis extending into myocardium	Epicarditis, focal myocarditis, and endocarditis
441	72	Epicarditis, endocarditis, and myocardial necrosis	Slight epicarditis

These findings suggest that serious injury to the dog's heart may occur when it is exposed to concentrations of potassium citrate used in the Melrose technique. In this experiment, factors of injury to the atrium from manipulation and infection were the same in the control side as in the atrium exposed to the potassium salt. Therefore, we suspect that the myocardial injury was due to direct effect of potassium citrate upon the heart muscle.

SUMMARY

1. A description is given of an experiment in dogs in which both atrial appendages were isolated for a short period. One appendage was used as a control while the other served as a closed pouch which was filled with potassium citrate solution for 30 minutes. The appendages were removed after varying intervals and examined microscopically.

2. Concentrated potassium citrate solution (25 per cent) caused myocardial necrosis in all 4 dogs that survived 24 hours or longer.

3. Dilute potassium citrate solution (30 mEq./L.) caused a more severe myocardial reaction than was found on the control side in 8 out of 11 animals. The 8 included 6 dogs with necrosis in the experimental pouch and 2 others with inflammatory reaction more severe than that found in the corresponding controls.

The authors are indebted to Mrs. T. Wiehe for her technical assistance with these experiments.

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SINUSAL STANDSTILL WITH VENTRICULAR AUTOMATISM DURING RETROGRADE PERFUSION OF THE CORONARY SINUS UNDER HYPOTHERMIA FOR DIRECT SURGICAL APPROACH TO THE AORTIC VALVES

An Experimental Study

C. Massimo, M.D., L. Boffi, M.D.,* and L. Pozzi, M.D.,***
Florence, Italy

DIRECT surgical approach to the aortic valves necessarily requires the uncovering of the aortic orifices of the coronary arteries. Therefore, we are faced with two fundamental difficulties: (1) the interruption of the coronary flow, and (2) the danger of coronary air embolism. In order to overcome these obstacles, employing the cardiopulmonary bypass technique at normal temperature, Lillehei and co-workers[1, 2] employed coronary perfusion during the intervention. At first this perfusion was effected through a direct cannulation of the aortic orifices of the coronary arteries; later on, the same authors preferred to use the retrograde coronary sinus perfusion. This technique enabled the surgeon to work directly on the aortic valves with safety, since the aortic orifices of the coronary arteries become temporarily transformed from arterial routes into venous routes. Almost at the same time, Blanco and his colleagues[3] developed a similar technique.

While the cardiopulmonary bypass, with the body at normal temperature, leaves the heart unharmed, the simultaneous use of the retrograde perfusion of the coronary circle can bring about several types of disorders of the heart rhythm, sometimes even ventricular fibrillation, as one deducts from the original article by Lillehei and from personal communication of Bailey.[4] Their interpretation seems to us unconvincing.

As a variation of the above-mentioned technique (retrograde coronary sinus perfusion with bypass at normal temperature), we have performed a retrograde perfusion of the coronary sinus under hypothermic condition with a technique already described by us in a preceding paper.[5]

In this short article we wish to illustrate an unusual disorder of the heart rhythm, which has constantly presented itself in all the experiments performed with the above-mentioned method. It is an arrhythmia which appears generally after 15 seconds to 40 seconds from the start of the inversion of the coronary circle; a sinusal bradycardia takes place and quickly increases until a complete stoppage of the atrioventricular activity is reached. Later on,

From the Santa Maria Nuova Hospital, Florence, Italy.
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*Department of Surgery, Santa Maria Nuova Hospital.
**Department of Cardiology, Santa Maria Nuova Hospital.

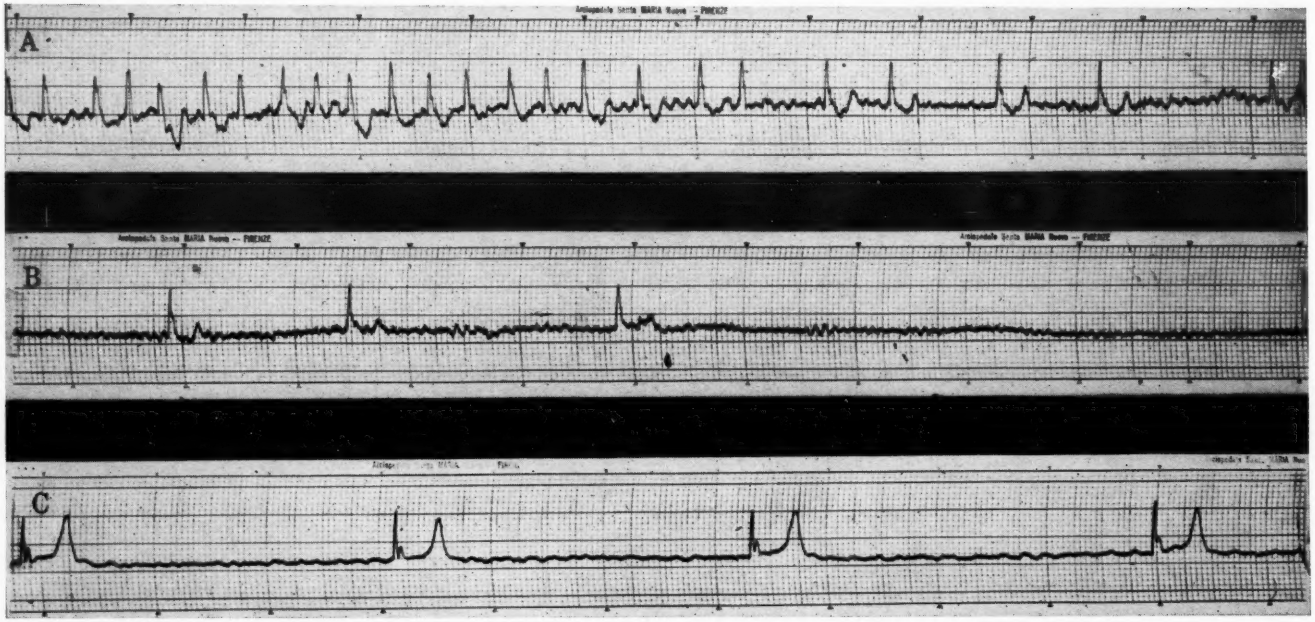

Fig. 1.—This electrocardiogram is from a patient who did not have sinusal standstill. Before the beginning of the retrograde coronary perfusion, an atrial fibrillation takes place with ventricular frequency of 180 systoles per minute (*A*). *B* shows the atrioventricular dissociation reached 15 seconds after the start of the retrograde coronary perfusion. The auricles continue to fibrillate while the frequency of the ventricles is 10 systoles per minute (as shown better in *C*).

an idioventricular center emerges which controls the ventricles with a regular frequency of 10 to 15 systoles per minute, while the auricles are in complete arrest. Sometimes this center can be disturbed by the presence of some ventricular extrasystoles. When the retrograde perfusion has ended and the normal coronary circulation has begun, the disturbance ceases and the sinusal rhythm starts again.

In some cases in which, during the preperfusional phase, owing to the sinus cannulation, the auricles had begun to fibrillate and the ventricular frequency had risen to 140 to 180 systoles per minute, the beginning of the coronary retrograde perfusion caused the sudden dissociation of the atrial activity from that of the ventricle. In fact, while the auricles continued to fibrillate, the ventricles were controlled on the low frequency which we have already mentioned (Fig. 1).

The meaning of this phenomena goes beyond our scope. We would like to mention that similar facts have been observed, either by employing some cardioplegic drugs (in particular, acetylcholine[6]), or by producing coronary ischemia by placing a clamp on the ascending aorta which will block the coronary orifices.[7]

It should be noted that, when the described technique has been used and ventricular fibrillation has appeared, it was observed only several minutes after the retrograde coronary perfusion had been interrupted and after the systemic circulation had been put into action again.

SUMMARY

A peculiar disorder of the heart rhythm is described which appears during the retrograde coronary sinus perfusion performed for direct surgical approach to the aortic valves under hypothermic conditions.

This arrhythmia is represented by sinusal arrest taking place 10 to 15 seconds after the start of retrograde coronary perfusion, while the ventricles are controlled by an idioventricular center, which was also present in those cases in which an atrial fibrillation was taking place.

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AN OCULAR SIGN USEFUL FOR EXPERIMENTAL SURGERY WITH PUMP-OXYGENATOR

G. N. Guastavino, M.D., J. A. Wikinski, M.D., R. H. Andres, M.D., J. Quinterno, M.D., and C. Donadei, M.D.,*
Buenos Aires, Argentina

AUTHORS in general agree on the possibility of acute lesions in the central nervous system during perfusion with a pump-oxygenator. In bypassing the heart and lung in the experimental laboratory, we routinely found an accurate sign of central nervous system lesions, which also proved to be of prognostic value. This sign was described in a previous paper[1] and further observations have confirmed this data. We believe this sign may be of interest to those working in the techniques of extracorporeal circulation. In the literature at hand we were unable to find any reference of this sign. For easier understanding we will present the behavior of the nictitant membrane (N.M.) and other ocular reflexes in the normal and conscious dog.

The conscious dog shows (a) very strong periorbital, palpebral, and conjunctival reflexes (the first of these has a large reflexological area and the most sensitive part is that near the internal ocular angle); and (b) the nictitant membrane (N.M.) is completely retracted over the internal ocular angle and is practically invisible, except for its pigmented free end. (Fig. 1, *A* and Table I.)

In the anesthetized dog under deep anesthesia (a) the N.M. is completely relaxed and covers a large surface of the ocular globe; this, together with convergent strabismus, causes the cornea and iris to be invisible; (b) the periorbital, palpebral and conjunctival reflexes are absent; and (c) the eyelids are closed (Fig. 1, *B*).

Under light anesthesia (a) the N.M. begins retraction and the end of the cornea is shown; periorbital and palpebral reflexes appear now, and will be stronger *even before* the N.M. is completely retracted (this is an important observation); and (b) the eyelids are still closed (Fig. 1, *C* and *D*).

In the almost awake dog (a) the N.M. is partially relaxed (more than 75 per cent of the cornea is seen); (b) very strong periorbital and palpebral reflexes are present (very slight friction produces blinking); and (c) the eyelids are closed (Fig. 1, *E*).

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*Head of the Department of Cardiac Surgery, Third Surgical Clinic, University of Buenos Aires, Hospital Ramos Mejía.

TABLE I

PALPEBRAL AND PERIORBITAL REFLEXES	N.M.	EYELIDS	MEANING
Positive	Totally retracted	Open	Awake
Negative	Totally relaxed	Closed	Deep anesthesia
Positive	Partially relaxed	Closed	Light anesthesia
Negative	Totally retracted	Open	Lesion in central nervous system

A pathologic sign, but a reversible one if its cause is rapidly attacked (prolonged hypotension, anoxic anoxia, microembolism, etc.), is that during the deep plane of anesthesia, as well as during light anesthesia (a) the N.M. begins quick retraction to the internal ocular angle; movement might frequently go on and finish retraction in a few seconds (when lesion is serious);

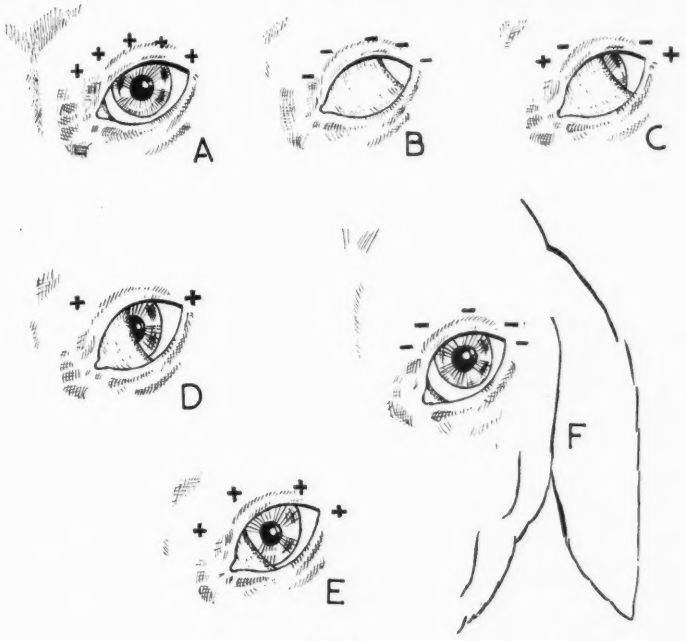

Fig. 1.

(b) there is absolute lack of periorbital and palpebral reflexes even if the N.M. has completely disappeared from the ocular field; corneal reflex is also missing; if anesthesia has been lightened before the accident, periorbital and palpebral reflexes disappear; and (c) the eyes are open and the animal seems to look but, of course, without seeing (Fig. 1, *F*).

If, upon noticing that the N.M. is retracting, the trouble is localized and solved (as has happened to us on many occasions when the pump-oxygenator operator and the surgeon were notified) the N.M. spontaneously relaxes again and it returns to the position it had before. Under these conditions the dog will behave as a normal animal.

In all normal cases as described above, perfect recovery of the dog is assured. It will awake, answer a call, perform coordinate voluntary movements, walk, and even eat. In the pathologic cases as described above, the dog will not awake. It will recover spontaneous breathing, arterial pressure will keep within acceptable levels, and it will even survive for several hours but it will actually be in a coma, similar to that produced by very deep anesthesia, but with a retracted N.M. and open eyes. It will feel no pain, perform no voluntary movement, and death will occur from respiratory or circulatory arrest.

SUMMARY

An ocular sign of prognostic value is described which has been observed in dogs during experimental cardiac surgery using a pump-oxygenator.

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COMPLETE DRAINAGE OF PULMONARY VEINS INTO THE CORONARY SINUS—LEFT SUPERIOR VENA CAVA COMPLEX

Daniel F. Downing, M.D., and Henry T. Nichols, M.D.,
Philadelphia, Pa.

ANOMALOUS insertion of all pulmonary veins into various components of the systemic venous system are being reported with increasing frequency. Surgical treatment has proved to be possible in some patients. To the list of operable variations of the basic abnormality we would add the situation encountered in a recently studied patient.

CASE REPORT

V. B., a 6-year-old girl, was found to have a cardiac murmur at the age of 2½ years. From the early months of life the parents had noted prominence of the left chest. She had always become fatigued and short of breath after brief exertion. Profuse perspiration was a feature even in cool weather. There had been no cyanosis, chest pain, syncope, cough, or signs of cardiac failure.

On physical examination the child was underdeveloped and undernourished. There was no cyanosis. There were no abnormal pulsations of the cervical vessels and the trachea was in the midline. The bony thorax was asymmetrical, the left anterior chest being more prominent than the right. The sternum was protuberant. The lungs were clear. The heart was not enlarged to percussion. There was no thrill. The cardiac rate was 96 per minute and there was a normal sinus rhythm. The second sound at the base to the left of the sternum was accentuated 1 plus. A short, harsh systolic murmur and an early diastolic blow were heard over the left thorax, best in the third interspace near the sternal border. The systolic murmur could also be heard over the right chest. The liver was not enlarged. Peripheral pulses were full. The height was 46 inches; weight, 41 pounds; blood pressure, 90/50 mm. Hg.

Laboratory data: There were 13.5 grams of hemoglobin. The hematocrit was 41 per cent. The electrocardiogram (Fig. 1) showed right ventricular hypertrophy. On films and fluoroscopy the pulmonary vascular markings were accentuated 2 plus. The main pulmonary artery was not clearly defined but was considered to be dilated. The heart was enlarged 2 plus, with rounding of the left border (Fig. 2). The right atrial segment was somewhat prominent. In the right anterior oblique view there was 2 plus anterior prominence and in the left anterior oblique, 1 plus anterior and 1 plus posterior prominence.

The data secured on cardiac catheterization are shown in Table I, A. When a catheter was introduced into a left antecubital vein, it passed via a persistent left superior vena cava to the right atrium and right ventricle. Re-introduced through a right arm vein, it passed through a right superior vena cava to right atrium, right ventricle, pulmonary artery, and coronary sinus. There was a marked step-up in oxygen content in

From the Department of Pediatrics and Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pa.
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the coronary sinus. This persisted through the right heart and pulmonary artery. Arterial oxygen saturation was normal. The mean pressure in the right atrium and the systolic pressure in the right ventricle and pulmonary artery were somewhat elevated.

On the basis of all the data, it was decided that a major portion of the child's pulmonary veins emptied into the left superior vena cava—coronary sinus complex.

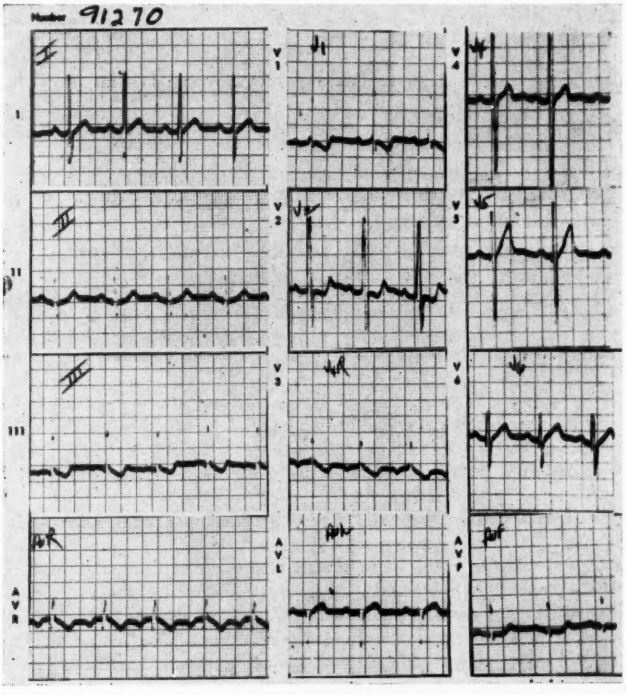

Fig. 1.

TABLE I. PREOPERATIVE (A) AND POSTOPERATIVE (B) CATHETERIZATION DATA

	A			B		
	O_2 CONTENT (VOL. %)	O_2 SAT. (%)	PRESSURE (MM. HG)	O_2 CONTENT (VOL. %)	O_2 SAT. (%)	PRESSURE (MM. HG)
AV				13.9		
RSVC	10.8			11.1		
LSVC (distal)	10.1			—		
LSVC (mid)	11.5			11.8		
IVC	11.3			13.6		
CS	16.8		(7)	5.1		(10)
RA h	15.2			12.1		
RA m	15.7		(7)	14.3 & 14.2		(0)
RA l	15.0			10.8 & 13.3		
RV l	15.8			14.4		
RV m	15.3		33/0	14.0		18/0
MPA	15.1		32/16	14.3		15/6
RPA	15.2			14.3		
SA	16.7	93.6	100/62	15.9	89.8	100/68

AV—axillary vein. RSVC—right superior vena cava. LSVC—left superior vena cava. IVC—inferior vena cava. CS—coronary sinus. RA h, m, l—right atrium, high, mid, low. RV l, m—right ventricle low, mid. MPA—main pulmonary artery. RPA—right pulmonary artery. SA—systematic artery.

On Aug. 20, 1956, she was operated upon (H. T. N.) through an anterior incision in the fourth left interspace. The left superior vena cava was found to be continuous with the coronary sinus, the proximal portion of the complex being hugely dilated. There was a localized continuous thrill over this area. The left pulmonary veins were dissected free and were found not to communicate with the left superior vena cava. A purse-string suture was placed in the wall of the coronary sinus and the structure explored with a finger. At the site of the thrill, a jet was felt which was found to issue from a single orifice, superiorly and posteriorly. Further exploration through this orifice indicated the presence of a chamber into which all pulmonary veins emptied. During this portion of the procedure, whenever the orifice was completely occluded, the patient would become very cyanotic. The finger could pass easily from coronary sinus to right atrium.

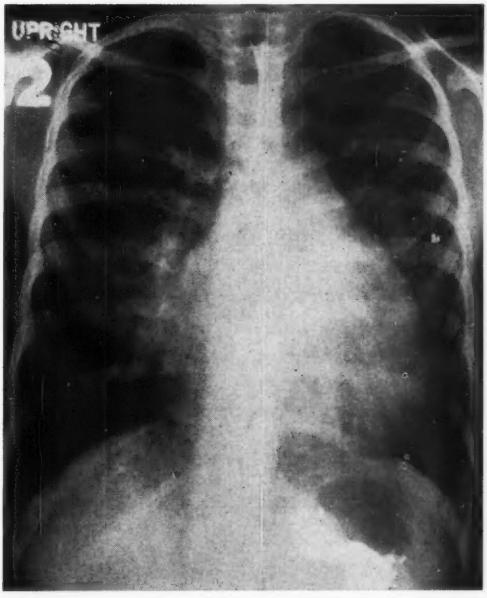

Fig. 2.

A purse-string suture was now placed in the wall of the left atrium near the appendage. The exploring finger encountered a normal mitral valve. No pulmonary veins emptied into the chamber. In the postero-superior portion of the interatrial septum, a defect, admitting the finger tip, was found. Each time this defect was blocked the peripheral pulse could not be palpated.

It was obvious that all pulmonary veins converged to form a "chamber" which communicated with the left superior vena cava—coronary sinus complex. Systemic circulation was possible only because there was an interatrial communication through which mixed blood from the right atrium could pass to the left atrium, left ventricle, and aorta (Fig. 3, *A*). Correction of the anomaly would involve the creation of a passage between the confluence of pulmonary veins and the left atrium and obliteration of that between pulmonary veins and coronary sinus.

The Nichols guillotine knife was inserted along the finger into the left atrium and the septum between it and the common pulmonary vein "chamber" incised as widely as

possible. Finger manipulation further enlarged this new passage and there was now relatively unobstructed flow of pulmonary vein blood into the left atrium. The communication between the common pulmonary vein and coronary sinus was then obliterated by multiple sutures (Fig. 3, *B*).

The postoperative course was uneventful and the child was discharged on the tenth day. Throughout the period, a moderately loud systolic blow was heard in the second and third left interspaces. The diastolic murmur was no longer present and the second sound at the base to the left of the sternum was normal.

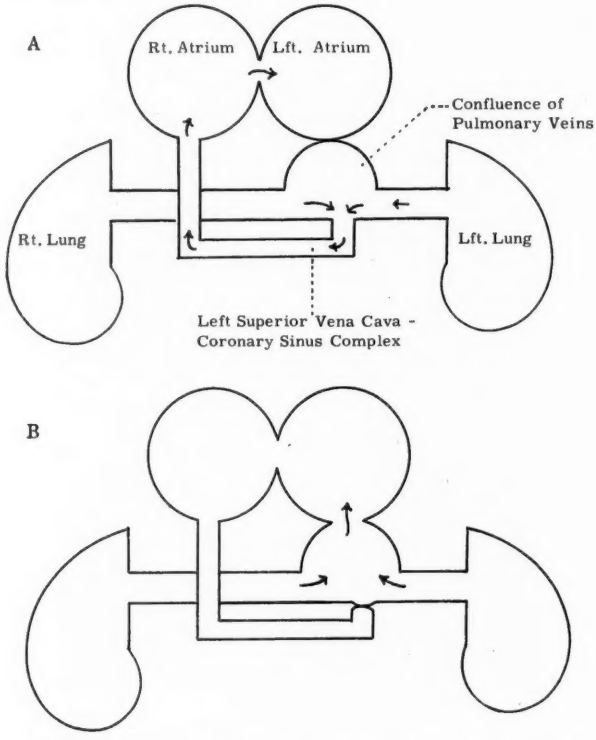

Fig. 3.—*A*, Course of the circulation before surgery. *B*, Course of the circulation postoperatively.

Second Admission.—Fourteen weeks later she was re-admitted. Full activity had been allowed after a period of one week at home and her exercise tolerance was now reported to be normal. She no longer would become short of breath on brief exertion. To the parents she appeared completely asymptomatic. On physical examination the systolic murmur was still present. She had gained 5 pounds.

Laboratory data: There were 13.3 grams of hemoglobin. The hematocrit was 43 per cent. The electrocardiogram showed no change. The data secured by cardiac catheterization appear in Table I, B. Cardiac catheterization was performed through the left brachial vein. On several occasions the tip passed through the coronary sinus into the left superior vena cava. There was no evidence of a left-to-right shunt into the left superior vena cava or the coronary sinus. Averaging all five venous inflow samples, there was a step-up of 1.8 volumes per cent in the right atrium. Leaving out the coronary sinus

sample, the step-up was only 0.3 volumes per cent. Ordinarily these figures would not be considered distinctive of a left-to-right shunt at the atrial level. However, the two samples from the mid-portion of the atrium contained a significantly greater amount of oxygen than did the other three, and the rise was continued through right ventricle and pulmonary artery. It was considered that there was a small left-to-right shunt at the atrial level. The pressure in the right atrium, right ventricle, and pulmonary artery was normal.

The result of operation is considered to be excellent. Unfortunately, there is evidence that the interatrial communication is still of functional significance. Whether this is an actual defect or a stretched patent foramen ovale is unknown. The eventual importance to the child also is unknown. However, it certainly does not pose the threat of the original condition.

DISCUSSION

The anomaly represents persistence of the common pulmonary vein trunk through failure of its absorption into the wall of the left atrium. Instead, it came to communicate with the left horn of the sinus venosus.

By some the patient would be described as having a triatrial heart. From our acquaintance with descriptions of "cor triatriatum" in the literature it seems obvious that most of these represent anomalous development of pulmonary veins rather than abnormal partitioning of the left atrium.

Once the anatomic situation is appreciated, the surgical therapy is relatively simple and can be performed rapidly. More effective than the incision and dilatation technique used in this patient would be an incision between the confluence of pulmonary veins and the left atrium followed by the use of a backward cutting punch and removal of tissue.

SUMMARY

In a 6-year-old child all pulmonary veins were found to drain into the coronary sinus at its junction with a persistent left superior vena cava. There was a small interatrial communication. A passage was created between the confluence of pulmonary veins and the left atrium; that between the confluence and the coronary sinus was then obliterated.

Postoperative catheterization demonstrated that the shunt into the coronary sinus was no longer present. There was now evidence of a small shunt from left atrium to right atrium. Pulmonary pressure, somewhat elevated before surgery, was now normal.

HUFNAGEL VALVE SURGERY FOR AORTIC INSUFFICIENCY

Technical Considerations and Report of Cases

William S. Conklin, M.D., Jerome T. Grismer, M.D.,** and Justin A. Aalpoel, M.D.,*** Portland, Ore.*

IT IS generally recognized that the prognosis of patients with severe aortic valve insufficiency is extremely grave. During recent years concerted effort has been directed toward discovery of a surgical solution for this problem. Of the various approaches that have been reported none has proved as successful as the one devised by Hufnagel—insertion of a plastic ball-valve into the descending thoracic aorta.

At best, the Hufnagel operation must be considered palliative since it fails to improve the hemodynamics of the coronary and brachiocephalic circulations. However, it does reduce by as much as 75 per cent the excessive work load to which the heart is subject in the presence of aortic regurgitation. In all probability, replacement of the damaged aortic valve with an acceptable prosthetic device will eventually be possible, thereby abolishing regurgitation completely. But considerable time must elapse before perfection and wide acceptance of such a procedure can be anticipated. In the interim, for those patients with clinical features warning of progressive deterioration and death, the potential benefits of a Hufnagel valve should not be denied. Patients in such a perilous state have a life expectancy of approximately 1 year, or even less, despite the most rigorous medical therapy. Although the surgical and late mortality of the Hufnagel operation has been high, the majority of the patients who survive the operation have been significantly benefited. Improvement in some has been dramatic.

Insertion of a Hufnagel valve into the descending thoracic aorta requires temporary cross-clamping of this vessel. Interruption of the distal aortic circulation for more than 15 minutes may result in irreversible spinal cord damage and other serious or fatal complications. In the animal laboratory and autopsy room, practice insertions can generally be accomplished easily and rapidly by simply excising a short segment of the aorta and pulling each end of the aorta over the appropriate end of the valve. In our early experiences with living patients, however, we soon encountered difficulties. The

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*Chief, Division of Thoracic Surgery, University of Oregon Medical School, Portland, Ore.
**Former Resident in Thoracic Surgery, University of Oregon Medical School. Present address: St. Louis Park Medical Center, Minneapolis, Minn.
***Resident in Thoracic Surgery, University of Oregon Medical School, Portland, Ore.

diseased aorta of these patients is likely to have lost its elasticity and to tear readily. On more than one occasion we lost valuable time when the short retracted lip of a divided aorta tore between the grasp of forceps that were being used to pull it over the cuff of a valve. For a while we tried to avoid the potential hazards of such a delay by placing a temporary bypass around the segment of aorta that was to be occluded during placement of the valve. Eventually, however, with suggestions contributed by various members of the operating team, a technique evolved which permits aortic occlusion to be limited to less than 5 minutes. Since we understand that others have been deterred from performing this operation because of difficulties similar to those which we have encountered, it seems worth while to report a technique which has permitted rapid placement of a valve, the aorta having been occluded, on occasion, for less than 3 minutes. The use of a temporary bypass is no longer considered necessary.

OPERATIVE TECHNIQUE

For the definitive part of this operation we consider that the operating team should include four surgeons and two scrub nurses. To each member of this group are assigned specific responsibilities and, for the benefit of those who may be inexperienced, these are rehearsed immediately before the aorta is clamped and the valve inserted. Constant vigilance on the part of the anesthesiologist and of the cardiologist who is monitoring the electrocardiographic equipment is obviously important.

The patient is operated upon in the right lateral decubitus position. A standard posterolateral thoracotomy incision is used and carried through the fifth intercostal space. Short posterior segments of adjoining ribs are resected, according to the need for increased exposure. It is sometimes helpful to use two rib spreaders, one at each end of the wound. Following exploration, the aorta is mobilized from the origin of the left subclavian artery distally, for a variable distance, depending on the length and diameter of the plastic valve that is selected for use. Dissection around the aorta may be tedious and time consuming, particularly when aortitis has produced a great deal of fibrous tissue reaction, as is not infrequently the case. It may be necessary to divide four or five pairs of intercostal arteries, as well as the bronchial arteries that are encountered.

We keep our Hufnagel valves and their multiple-point fixation rings continuously sterile by storage in 1:700 Zephiran solution. At least one of each of the four standard sizes should be available for every operation.* At the operating table the valves are washed and placed in a solution containing 100 mg. of heparin to 500 ml. of normal saline. It is important that the valves be handled only with the special valve holder* and that scratching or marring

*Formerly we kept two valves of each size on hand so a replacement would always be available. We found, however, that the number and urgency of these operations did not require this. The valves are obtained from Brunswick Mfg. Co., 61 Hampshire St., Boston 20, Mass.; the valve and ring holders from Geo. P. Pilling & Son. Co., 3451 E. Walnut St., Philadelphia, Pa.

of the inner surfaces of the valve or the valve edges be avoided. A defect on a surface that is exposed to the blood stream may prove to be a site for thrombus formation.

The largest usable valve should be selected; but one should avoid choosing one that is too large, since time may be lost during unsuccessful attempts to introduce it. One must take into consideration, too, the length of the valve and the amount of the aorta that will be resected, in order to prevent kinking of the vessel after the valve has been inserted. Since the maximum diameter of the valve is greater than that of the aorta, the reconstituted vessel will be displaced to the left. If too much of the aorta is resected there will be greater

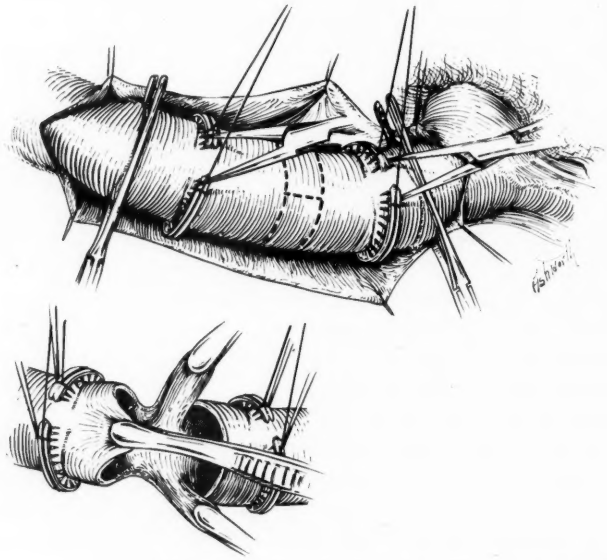

Fig. 1.—Preparation of descending thoracic aorta for placement of Hufnagel valve.

difficulty in placing the valve and excessive kinking where the proximal end of the aorta joins the valve. The same will be true if the valve is placed too close to the aortic arch. We have never found it necessary to resect more than 2 cm. of the aorta, no matter how long the valve. Sometimes there can be considerable discrepancy in the size of the aorta at its two divided ends, particularly in persons who have had syphilitic aortitis with proximal dilatation of the vessel. Under such circumstances it may be desirable to place the valve in a more distal position, where the aorta is more uniform in size. In any case, the smaller end of the aorta must be used as a guide to selecting the size of the valve that will be inserted.

The two nylon multiple-point fixation rings of the selected valve are prepared in advance by anchoring a strand of heavy silk (No. 3) into the circumferential groove of each with four or five fine silk ligatures. These

rings are then placed around the proximal and distal ends of the mobilized segment of aorta. A special ring-holding clamp with a ratchet is attached to each of these rings and the clamps are held open by the assistants who have been selected to close the rings over the cuffs of the valve after it has been inserted. Large Potts clamps (straight, angled, curved, or spoon-shaped, according to ease of placement) are also held open, proximal and distal to the rings, ready for occlusion of the aorta and isolation of its mobilized segment (Fig. 1). Another assistant holds one of two aspirators, ready to remove any blood that appears in the operative field. The surgeon holds long, straight scissors (Nelson) in one hand and Russian forceps in the other. The instruments that may be needed are so placed as to be immediately available, all others being set aside. The surgeon then reviews the responsibilities of each team member and asks the anesthesiologist and cardiologist for an evaluation of the patient's condition.

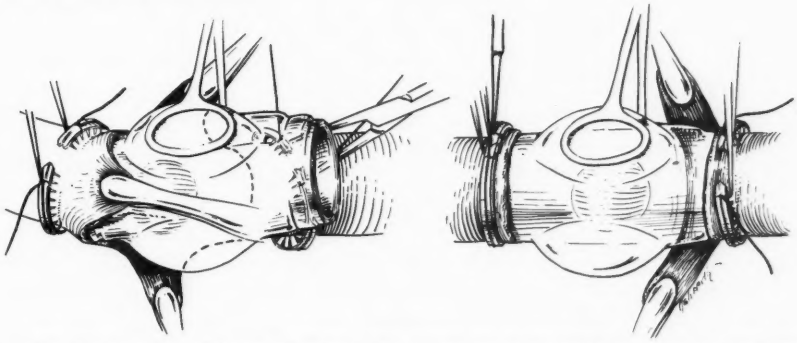

Fig. 2.—Insertion of Hufnagel valve. The lateral lip of the aorta is better elevated over the valve cuff with 2 or 3 pairs of forceps. After the aorta has been completely divided, a Semb forceps (sharp curve) serves well to grasp the free medial segment for traction while inserting the proximal end of the valve.

At a signal from the surgeon, who has assured himself that everything is in good order, the aorta is occluded first at the proximal end and then at the distal end of the isolated segment. The following steps are next carried out, deliberately, avoiding haste:

1. The aorta is *partially* transected (about two-thirds) with Nelson scissors at the two points, 1 or 2 cm. apart, at which the ends of the valve will be introduced.
2. A longitudinal cut is then made between the two partial transverse cuts, dividing the intervening segment of the aorta into two equal "side straps" (Fig. 1).
3. The surgeon is handed the selected valve in the valve holder, and he checks to make sure that the valve is properly positioned.
4. The surgeon slides the distal end of the valve along the medial (uncut) wall of the aorta into its open distal end, as he and an assistant lift the cut, lateral portion of the aortic wall over the cuff of the valve and past its groove with two pairs of Russian forceps (Fig. 2).

5. When this end of the valve is snugly in place, with sufficient aortic lip over the edge of the valve, the selected assistant brings up the plastic ring and secures the aortic lip in the groove of the valve cuff by closing the ring-holding clamp. The ratchet of the clamp locks the ring in place.

6. The surgeon divides the remainder of the aorta at the site of the distal transverse cut. Potts 60-degree scissors are useful for this purpose. The proximal stump of the aorta retracts cephalad. Still attached to it is the segment of the aorta which will be resected and this segment will serve as a very useful "handle" and "guide" for the next step.

7. The end of this segment is grasped in a Semb forceps (sharp curve), or its "side straps" are grasped with two pairs of Russian forceps, and traction is applied to it. Using its medial surface as a guide, the surgeon slides the proximal end of the valve into the corresponding aortic stump, the lateral free edge of the aorta again being lifted onto the valve cuff with forceps.

8. The proximal end of the aorta is fixed to the valve cuff with the multiple-point fixation ring, as was done at the distal end.

9. The surgeon punctures the aorta close to the valve with a 20-gauge needle on a Luer-Lock syringe which has been partially filled with dilute heparin solution. He attempts to fill the valve chamber with the solution, aspirating as much of the contained air as possible.

10. The syringe is removed and the open needle is held in place with a clamp so that residual air may escape through it as the *distal* Potts aortic clamp is opened and blood enters the valve from below.

11. The proximal Potts aortic clamp is opened *gradually*. The valve immediately begins to function. It is felt that this proximal clamp should be opened over a period of perhaps 3 to 5 minutes, depending on changes in cardiac rhythm and rate, and on the response of the blood pressure. Since aortic circulation has been re-established, time is no longer a primary factor.

12. As soon as possible, the heavy silk ligatures in the grooves around the valve rings are tied, even before the proximal aortic clamp is completely opened or removed. This permits removal of the ring holders. Stainless steel wires (No. 26) are then threaded through the holes in the rings and tied, to hold the rings securely and permanently in place.

During the period that the aorta is clamped, even though brief, the blood pressure proximal to the clamp may rise to extreme heights. On occasion we have used a short-acting hypotensive drug (Arfonad) to counteract this. Should marked tachycardia or drop in blood pressure occur after the aortic clamps have been removed it may be advisable to recompress the aorta, at least partially, until stabilization results.

We have not encountered major bleeding from the aortico-valvular junctions. Some bleeding has occurred from between the fixation points, particularly at the proximal end of the aorta when it is significantly larger than the distal end. Such bleeding is readily controlled by tightening the cuff with 4-0 arterial silk sutures or by the next step, which is carried out in any case. This involves placing strips of Ivalon sponge or plastic fabric about the aorta, above and below the valve rings, so as to tighten the aortic walls snugly to the free ends of the valve which protrude beyond the rings into the lumen of the aorta. As Hufnagel has indicated, these tightly sewn strips obliterate the groove between the aortic wall and valve edge, decreasing the likelihood of thrombus formation at these sites. If these strips cover the valve rings as well as the valve ends, they are less likely to slip out of position.

In the past we have also sewn a sheet of Ivalon sponge around the main portion of the valve, believing that this served to muffle the noise of the valve to a considerable extent. The Ivalon sheet will no longer be necessary for this purpose, since "silent" valves are now available. But it may still have some value in that it serves as padding between the valve and the spine and it also helps in anchoring and stabilizing the valve, since the pleural edges can be sutured to it. A single sheet of sponge can be used for both purposes—to cover the valve and to cinch up the aorta around its ends. The remainder of the operation does not differ from other major thoracotomies. We have used closed pleural drainage routinely.

The postoperative management is similar to that of other major thoracic operations. Drainage tubes can generally be removed within 1 to 3 days. We have felt that routine use of prophylactic antibiotics is desirable, because of the foreign bodies that have been introduced. We have not used anticoagulants, but it may prove advisable to do so. There seems to be a tendency for the red blood count to drop off during the early postoperative course, possibly due to valve trauma. Hematologic studies should therefore be carried out at frequent intervals until the red count and hematocrit have become stabilized. It has been our arbitrary practice to defer ambulation and hospital discharge for these patients longer than for most. Gradual ambulation has generally been started on about the third postoperative day and most of the patients have been discharged near the end of the second week.

SURGICAL RESULTS AND EXPERIENCES

Our experience with Hufnagel valve surgery includes 21 cases between the ages of 10 and 63. Of these, 3 were in the second decade of life, 3 in the third, 4 in the fourth, 7 in the fifth, and 2 each in the sixth and seventh decades. All had severe aortic regurgitation, and all but 1 had developed signs and symptoms of ominous import. The child of 10, originally explored for a patent ductus arteriosus, was found to have a sinus of Valsalva aneurysm which was obliterated with mattress sutures over pieces of Ivalon sponge. Retrograde aortography during the operation and angiocardiography after it failed to reveal a rupture of the aneurysm with a left-to-right shunt. Because

of severe aortic regurgitation, attributed to a dilated valve ring (Marfan's syndrome), a Hufnagel valve was inserted 2 months later. The child's response to this surgery has been considered good. In 5 of the remaining patients, aortic insufficiency was attributed to syphilitic aortitis. Rheumatic aortic valvular disease was considered the basic etiology in the remaining patients.

Three patients died on the operating table with terminal ventricular fibrillation and asystole. In one of these the ventricular fibrillation appeared *during* a 4 to 5 minute occlusion of the aorta. In the second, it occurred after the valve was functioning, following a 10-minute occlusion of the aorta. The third patient, 61 years old, had had a left pneumonectomy for chronic suppurative disease, with multiple lung abscesses, 2 years previously. At autopsy, he was found to have severe aortic insufficiency, moderate aortic stenosis, mild mitral stenosis and insufficiency, severe generalized arteriosclerosis, and moderate coronary sclerosis. Total aortic occlusion had lasted 15 minutes. Cardiac arrhythmia first developed several minutes after good valve function had been established. In an early case, death occurred on the third postoperative day with acute renal shutdown and paralysis of the lower extremities. Her aorta had been occluded for a prolonged period due to technical difficulties. A recent 63-year-old patient died a week following surgery with acute fulminating septicemia.

In addition to the 5 hospital deaths there have been 4 late deaths. In one of these, death was not directly related to the valve disease or to the Hufnagel operation, which had been performed a year and a half previously. Death was due to peritonitis which followed gastrectomy for ulcer and a secondary laparotomy for acute bowel obstruction. This patient did, however, have thrombosis of the right external iliac artery which had begun to manifest itself before the gastrectomy was performed and is presumed to have been embolic in origin. Another patient died a year postoperatively with acute bacterial aortitis. This patient, although improved early, had increasing anginal pain. His family physician referred him to a neurosurgeon who performed a thoracic sympathectomy which was complicated by an empyema. The aortitis developed soon thereafter. A patient who had had a bowel resection for mesenteric thrombosis 1 month following his Hufnagel operation died suddenly 3 months following it, while visiting with a friend. His "valve noise suddenly stopped." He had had previous episodes of arrhythmia and it is believed that terminal ventricular fibrillation occurred. The fourth patient died in a shock-like state, with cold, pulseless lower extremities, 5 months following surgery. Permission for autopsy was refused.

Of the 16 patients who survived the operation and left the hospital, all were considered to be at least temporarily improved. All those who still survive, except for the most recent one, have returned to their previous occupations. Since the prognosis of almost all these patients was considered to be extremely grave, we consider the over-all salvage to have been gratifying,

despite the high early and late mortality. An 18-year-old boy was the only patient whose prognosis without surgery was thought to be relatively good and he has done exceptionally well. All of the others had been in failure or they had severe angina, episodes of syncope, or both. The first of these patients, a 50-year-old Negro man, was operated on in April, 1954. His response was excellent and has been maintained, although he has been rehospitalized several times for acute alcoholism.

The high incidence of thromboembolic complications, early and late, presents a serious problem. These probably occurred in 5 of the 21 patients. The incidence has been lower since our present technique became established in January, 1956 (1 in 9), but these patients have not been followed for as long a period of time. Our experience does indicate that early operative mortality is related to the length of aortic occlusion. There were no operating room deaths among the 9 patients operated upon by our present technique and the only hospital death was due to septicemia. Aortic occlusion was limited to 5 minutes or less in all of these patients except 1. In this case, one of the multiple-point fixation rings of the selected valve proved to be defective. Despite having been tightly fixed in position, it twice slipped off the valve cuff, with loss of considerable blood. A different ring was employed for the third fixation and this held securely. The patient, who has made a good recovery, had three periods of aortic occlusion, totaling perhaps 12 to 15 minutes. There were, however, periods of aortic blood flow between occlusions. Since this experience, when a nylon ring seems to fit too loosely we now take the precaution of shaving off, with a scalpel, a little of the plastic from the notches at its ends.

It is not unusual for a surgeon to be discouraged by his early experiences with a new technique and to find that results improve as its potentialities are further explored and more and more of the pitfalls are avoided or overcome. Accepting the fact that this operation is not ideal, in that it does not correct the physiologic problem completely, we are convinced that it does have proved value and that it should continue to be recommended for patients who are not likely to survive, until a more completely restorative procedure becomes available. We recognize that the mortality has been very high. We believe that it will be less high in the future. The operative risk will doubtless remain great for the patients most urgently in need of help—those with very large hearts, in chronic failure, etc.—no matter what surgical procedure may become available. For such patients, however, a considerable risk seems acceptable if an operation offers better than a 50 per cent chance of prolonging their lives and relieving their symptoms.

SUMMARY

We have performed the Hufnagel operation for aortic insufficiency on 21 patients. Three of these patients died on the operating table with terminal ventricular fibrillation. In addition there were 2 hospital deaths and 4 late deaths. In 6 or 7 of these patients (about 33 per cent) death can be attributed

directly to the operation and its complications. Experience indicates that refinements in technique will go far toward reducing this high mortality. The technique which we presently use is described.

The 12 patients who survived have all been significantly improved and, except for the most recent one, have returned to their previous occupations. We believe that until an operation is devised which can abolish the regurgitation completely, with as great or greater safety, the Hufnagel operation should be recommended for patients with severe aortic regurgitation who have developed ominous signs.

ADDENDUM

Two additional patients are doing well over 3 months following their operations. On the other hand, a young man of 20 years of age, who was the most recent of the cases reported above, after marked initial improvement, developed a fulminating septicemia and at autopsy was found to have a large thrombus in the valve.

One of the authors (W. S. C.) has proposed that insufficiency could be eliminated for all but the coronary circulation if end-to-side shunts were introduced from below the Hufnagel valve to the innominate and left common carotid arteries, after which these vessels and the left subclavian artery would be divided. Preliminary work with animals for development of such a technique has not been carried out and it does seem that successful excision and replacement of the aortic valve proper, under cardiac bypass, will be developed and should provide a better solution to the problem.

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SOME CLINICAL AND PATHOLOGIC ASPECTS OF COARCTATION OF THE AORTA AND AORTIC ARCH SYNDROME

A. Temesvári, M.D., and A. Árvay, M.D., Budapest, Hungary

MANY PROBLEMS concerning the coarctation of the aorta remain unsolved. The area of coarctation and the pathology of the coarctation proper have been the subject of extensive studies. However, very little attention has been paid to changes in other parts and in the branches of the aorta. The problems concerning the collaterals, which are so important from the point of view of surgery, are far from being solved.

It is assumed that aortic coarctation is caused by a developmental disorder which occurs during the early weeks of intrauterine life by the failure of union between the parts of aorta growing from the heart anlage and those from the blood islets. This explains the various forms of coarctation, the various localizations, as well as the frequently observed changes in other blood vessels, such as the branches of the aortic arch and the intercostal arteries.[1] We believe that the developmental disorder will not always be restricted to the area of coarctation proper. Variable changes will occur in the ascending aorta, the immediate prestenotic segment as well as the post-stenotic area. In such cases the ascending aorta is either normal or hypertrophic, while the segment immediately proximal to the site of coarctation is often hypoplastic in its entire length, in spite of the fact that systolic pressure is much higher than in the post-stenotic area. In addition, the postcoarctation area itself is also abnormal; early in its development it shows hypoplasia, while later on secondary degeneration develops as a result of diminished pulse amplitude, affecting mainly the media.[2] The weakened vascular wall is then locally dilated by the vortex effect leading sometimes to aneurysm formation and rupture.[3]

The development of the postcoarctation dilatation may be traced back to the following causes.

The changes occurring in the uppermost, dilated intercostal arteries, which serve as collaterals, cannot be considered to be due to a simple compensatory effort or to an hypertrophy. It has been found that within 3 to 4 cm. from the aorta, these arteries are thin walled, excessively dilated, and do not pulsate. For this reason, the ribs in this area show no erosion. In these segments, the media is richer in elastic fibers and elastic elements are relatively more abundant than muscular elements when compared with the media of normal, muscular-type intercostal arteries (Fig. 1). Peripheral to this segment the intercostal arteries are thinned and a true "stricture" is visible in an area

From the Department of Cardiovascular Surgery, National Institute of Cardiology, Budapest, Hungary.
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a few centimeters in length, distal to which another relatively dilated segment occurs; in the latter area the vascular wall is thicker, the vessel pulsates intensively and is tortuous, forming multiple loops. This latter vascular segment anastomoses with the collaterals coming from the back muscles; the costal erosion is caused by the loops and their pulsation. The segment peripheral to this is narrowed again until it reaches the internal mammary artery.

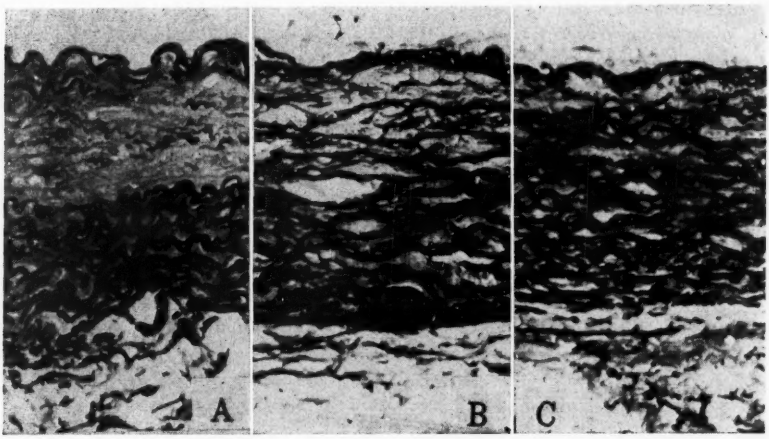

Fig. 1.—*A*, Normal intercostal artery (control).
B, Dilated collateral intercostal artery with a diameter of 6 mm.
C, Dilated collateral intercostal artery with a diameter of 8 mm.

Fig. 2.—The para-aortic segment of a dilated intercostal artery below the site of coarctation. Post-mortem specimen.

Thus, in the single intercostal collateral there are two narrowed and two dilated segments (Figs. 2 and 3). It is believed that here, too, the strictures arose at the sites of union of segments grown from a single anlage. The two dilated segments differ in behavior; the one next to the aorta does not pulsate, while the peripheral, convoluted one shows marked pulsation. We have been unable to find in the literature any explanation of this phenomenon. It is

equally unknown why a certain area of these vessels is of such a tortuous course. As one tries to interpret these observations one is not even certain whether in every intercostal collateral artery, or throughout its course, the direction of blood flow is toward the aorta. These problems have been subjected to further study.

Not infrequently the left subclavian artery or the other major branches of the aorta show signs of hypoplasia, similar to those seen in the intercostal arteries. The left subclavian artery is frequently stenosed or totally obliterated. However, this is restricted to only one segment of the vessel. The

Fig. 3.—The peripheral narrow (*A*) and the convoluted distal (*B*) segments of the intercostal artery shown in Fig. 2.

Fig. 4.—D. A., male, aged 25 years. Hypoplasia of the left subclavian artery. Photographed during operation.

obliteration is often not at the site where the artery branches off from the aorta but a few millimeters distal to it. The artery resumes its normal diameter in most cases at the site of its division, resulting in a dumbbell pattern (Fig. 4).

This type of stenosis affecting the big arteries branching off from the aorta, as it occurs in association with coaretation of the aorta, presents a pattern closely similar to that seen in cases of aortic arch syndrome. Although it is unquestionable that the latter may also be due to arteriosclerosis and/or

arteritis, the close resemblance makes it quite likely that in some of the cases of aortic arch syndrome a developmental disorder similar to that occurring in coarctation might be involved. Here, too, the stricture may develop at the site where the vascular buds growing from the different blood islets unite and this would explain also the segmental, circumscribed nature of the abnormality. The pathologic change might develop in two stages. The primary change would be a developmental disorder arising during intrauterine life. The secondary lesion would be an inflammation affecting the histologically inferior hypoplastic vascular wall ("locus minoris resistentiae") later in life.

In one of our cases of aortic syndrome, histologic study has revealed that in the area of segmental obliteration, especially in the intima, the smooth muscle elements increased in number and showed unusual distribution, the isolated smooth muscle cells were surrounded by rings of fibroelastic tissue (Figs. 5, 6, and 7). These changes suggest the presence of a disorder of tissue development in the intima (hamartosis) that made the vascular wall susceptible to infection and thrombus formation.

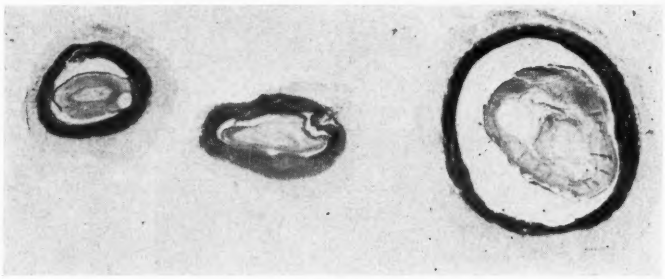

Fig. 5.—Cross section of the innominate artery (big diameter), the subclavian and the common carotid arteries. In all three vessels, the media had been detached circularly from the intima, as a result of operation. The lumen was filled with organized thrombus, showing small-caliber recanalization.

The correlation of these pathologic observations with clinical and surgical findings leads to the following practical conclusions.

Considering the different segments of the coarctated aorta, the surgical significance of the changes affecting them will be seen as follows. The ascending aorta is of no significance as far as surgery is concerned. On the other hand, both the pre- and the postcoarctation segments are of decisive significance. In one of our patients (I. B., male, aged 17 years) it was found at operation that the precoarctation part of the aorta (about 2 cm. long) showed hypoplasia and a diameter much smaller than normal. The subclavian artery had the diameter of an index finger and its wall, like that of the aortic arch, was sclerotic. After resecting the coarctated part of the aorta, an end-to-end anastomosis was done. Both above and below the coarctation the aorta was clamped by using a Crafoord clamp at each site. Owing to lack of space, the proximal clamp had to be placed higher on two occasions. When the anastomosis was completed it was found that at the site where the Crafoord clamp was first applied it had completely severed the intima and media of the aorta, which had been pulled apart by tension; this defect was bridged only by the adventitia. For this reason the anastomosis had to be resected and a new

anastomosis performed. This, too, was damaged. The two failures forced us to free the subclavian artery, to cut it high, proximal to where it divided and, by pulling the end down, to create an anastomosis between the subclavian and the distal part of the aorta. The thick postcoarctation aortic wall was not damaged by the Crafoord clamp. The patient made an uneventful recovery and was discharged 3 weeks later.

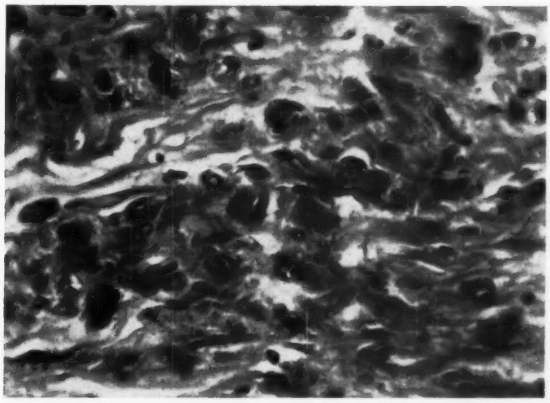

Fig. 6.—High-power view of the junction between intima and thrombus. In the fibrotic matter disarranged, isolated smooth muscle cells can be seen. These do not form bundles, but lie in different directions separated by fibroelastic tissue.

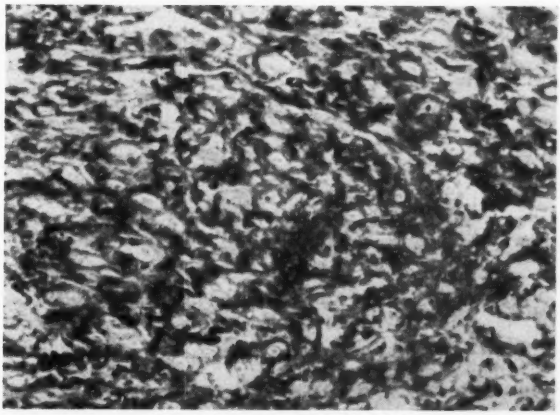

Fig. 7.—High-power view of the fine fibroelastic network separating the disarranged smooth muscle cells the nuclei of which can be seen faintly in the meshes of the elastic fibers (Weigert's elastic stain).

An anastomosis made with the hypoplastic aortic precoarctation segment may lead to even more serious complications. The precoarctation aortic segment of N. S. (male, aged 20 years) showed hypoplasia while the postcoarctation segment was enormously dilated. After resecting the coarctated part, the two aortic ends were united by an end-to-end anastomosis. No bleeding was seen after the release of the clamps and no complications were noted during

the operation. Three weeks later the patient was discharged free of complaints and was admitted to a department of internal medicine, where he spent an additional 5 weeks without having any significant complaints. He then developed left thoracic pain. A few hours later he suddenly spit a mouthful of blood and collapsed. After developing severe dyspnea, the patient died in a short time. At necropsy a small apple-sized, partly fresh and partly old hematoma was found at the junction of the arch and the descending aorta, surrounded by a connective tissue capsule, 2 to 3 mm. thick. At one point the connective tissue wall had broken through into the left superior lobe of the lung. At the dissection of the aorta it was seen that on the precoarctation side of the suture line there was a smooth opening, through which one could enter the sac of the hematoma. Higher up, in the precoarctation segment, where it was damaged by the Crafoord clamp, there was a semilunar area covered on the outside by the adventitia and on the inside by newly grown endothelium. This, however, was not the cause of the hematoma (Fig. 8). A similar

Fig. 8.—N. S., male, aged 20 years. Post-mortem specimen. The insufficient part of the suture line (*A*) and superior to it the impression made by the Crafoord clamp (*B*) are visible.

cause was responsible for the fatal outcome of another of our cases, 59 days after operation. The conclusion that can be drawn from these 3 cases is that an end-to-end anastomosis using a hypoplastic precoarctation segment, especially under tension, may lead to very grave consequences. In the 2 latter cases, the sutures placed in the hypoplastic precoarctation aorta wall held well for some time, but a few weeks later single sutures cut the wall as a result of increased pulsation and tension. This took place in the precoarctation segment only, while in the postcoarctation segment no damage was caused either by the sutures, or by the Crafoord instrument. For this reason we have recently decided to use a Blalock clamp on the precoarctation segment, placing

it anterior to the subclavian artery; thus, it cannot slip and need not be closed tightly. The practical importance of late suture insufficiency is best illustrated by the fact that we have lost a total of 4 out of 20 patients operated upon, 2 of the 4 because of this complication.

The collaterals which open into the postcoarctation segment tear easily and can be ligated only with difficulty. When they are ligated too close to the aorta, the silk thread may cut them off the thick, hard aortic wall. When ligated more distally, the increased pulsation after the anastomosis has been made may rupture the stumps, resulting in a serious hemorrhage. Hence they should be ligated very carefully, near to the aorta if possible, but taking precautions to prevent their being torn off. In view of these difficulties Crafoord[4] has recently decided not to free these vessels and not to resect them. Thus, the postcoarctation segment is not mobilized and the complications due to damage to the collaterals are avoided.

In D. A., a 25-year-old male, the subclavian artery showing hypoplasia had been resected to ensure an increased mobilization of the aortic arch and precoarctation segment. The latter, too, showed hypoplasia and, on the aortic arch, a circular detachment was visible proximal to the left common carotid artery. After the coarctated area had been resected, the two ends were united by end-to-end anastomosis. As a result of the resection of the subclavian artery and mobilization of the aortic arch, the sutures were not under tension. The patient tolerated the operation well and was discharged 2 weeks later, recovered. The interesting feature in this case is the simultaneous occurrence of aortic maldevelopment and subclavian hypoplasia. Although the latter had proved to be passable on retrograde catheterization, it could not have played a significant part in function, as the patient had no collateral circulation on the left side, which accounts for the absence of rib erosion there. Thus, the hypoplasia of the subclavian artery has the clinical significance that its resection represents no substantial loss and therefore it is worth while to sacrifice it in order to ensure a better mobilization of the precoarctation aortic segment.

SUMMARY

In the studies made thus far we were concerned mainly with those changes which occur in cases of coarctation outside the coarctated area: in the pre- and postcoarctation segments of the aorta, in the branches of the aortic arch and in the collaterals. Analyzing these one by one in the light of pathologic evidence, we have endeavored to show that all these rather neglected and ignored anatomic changes may play roles of considerable importance in the surgery for coarctation of the aorta, may profoundly influence our choice of the best surgical method, and may be of decisive importance in the outcome, favorable or unfavorable, of operation.

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DEHISCENCE OF THE DIAPHRAGM ASSOCIATED WITH FRACTURES OF THE PELVIS OR LUMBAR SPINE DUE TO NONPENETRATING WOUNDS OF THE CHEST AND ABDOMEN

Robert I. Carlson, M.D., Walter L. Diveley, M.D., Walter G. Gobbel, Jr., M.D., and Rollin A. Daniel, Jr., M.D., Nashville, Tenn.

IN THIS day of ever-increasing horsepower in the automobile engine, we may expect to encounter an increasing number of patients subjected to particularly violent trauma. We have recently seen 2 patients with extensive fractures of the pelvis and lumbar spine in whom dehiscence of the diaphragm also occurred. This prompted a review of our experience, and of similar cases reported in the American and British literature from 1946 through 1957, inclusive. Our interest is limited to those cases in which sudden and markedly increased intra-abdominal pressure caused the diaphragm to rupture. Cases in which there was an associated penetrating wound or in which the diaphragmatic injury was thought to be due to a fractured rib fragment were excluded.

RESULTS

In the review of patients treated at the Vanderbilt University and Thayer Veterans Administration Hospitals from 1946 through 1957, 9 patients with dehiscence of the diaphragm caused by nonpenetrating trauma were encountered. In 6 of these 9 patients, a fracture of the bony pelvis and/or the lumbar spine was also found. Seven of the 9 patients were males and all 9 patients recovered. Summary of the findings in those with fractures of the pelvis and/or lumbar spine, together with the pertinent x-ray studies, are presented in Figs. 1 through 6.

Although the interval between the accident and the patient's admission to the hospital ranged from 2 hours to 4 days, exploration was carried out in all patients within 5 hours after admission to the hospital. In 3 instances, a thoraco-abdominal approach was used; in 5 cases concomitant but separate incisions were made into the chest and the abdomen; and in 1 case the hernia was repaired through a thoracic incision. In 3 of the 9 cases, intra-abdominal injuries were found which required surgical care. In 1 case a lacerated spleen was removed. In the second case, a laceration of the left lobe of the liver required suture; and, in a third instance, a complete transection of the distal

From the Surgical Service, Thayer Veterans Administration Hospital, and the Department of Surgery, Vanderbilt University Hospital, Nashville, Tenn.

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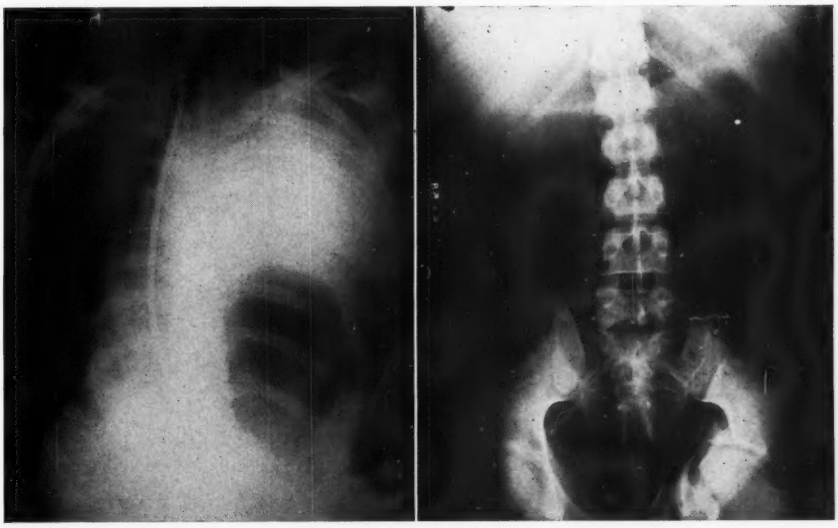

Fig. 1.—Age—27. Year—1953. Etiology—auto crash. Interval Prior to Hospitalization—3 days post-trauma. Extent of Diaphragmatic Tear—10 cm. Associated Injuries—laceration of stomach.

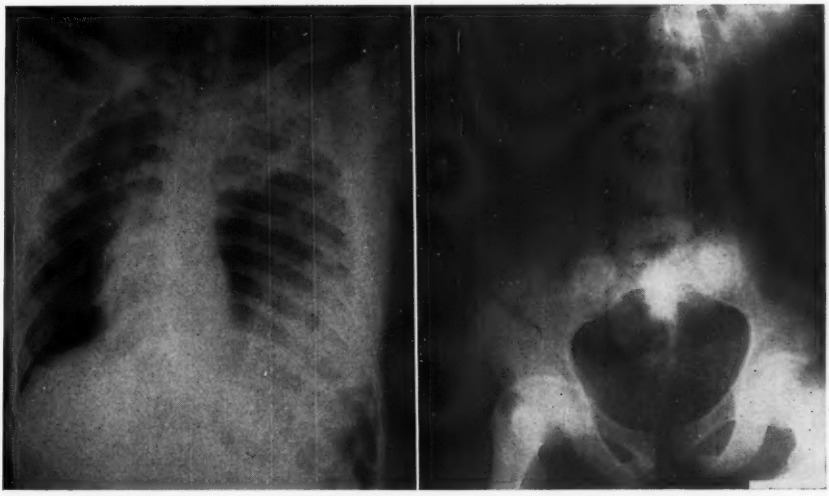

Fig. 2.—Age—22. Year—1953. Etiology—mine accident. Interval Prior to Hospitalization—36 hours post-trauma. Extent of Diaphragmatic Tear—14 cm. Associated Injuries—none.

ileum was found. This experience emphasizes the necessity for adequate exposure of both the chest and the abdomen in order that a complete exploration may be carried out. In all 9 cases, recovery from the procedure was

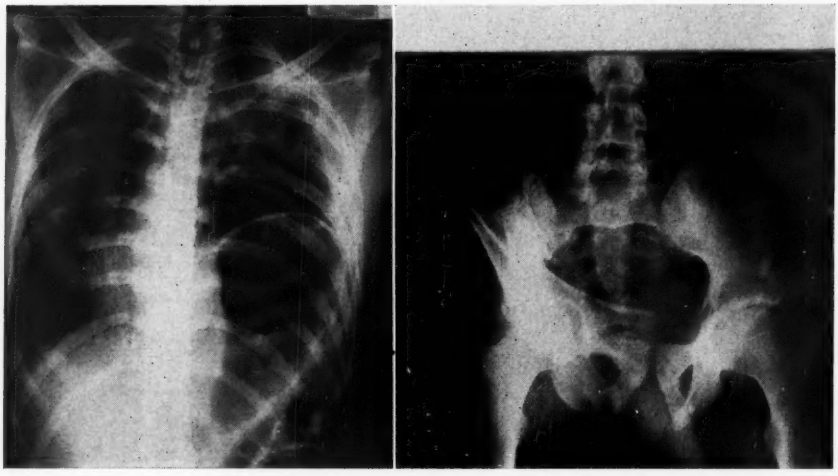

Fig. 3.—Age—20. Year—1955. Etiology—run over by car. Interval Prior to Hospitalization—2 hours post-trauma. Extent of Diaphragmatic Tear—16 cm. stellate. Associated Injuries—transection of ileum.

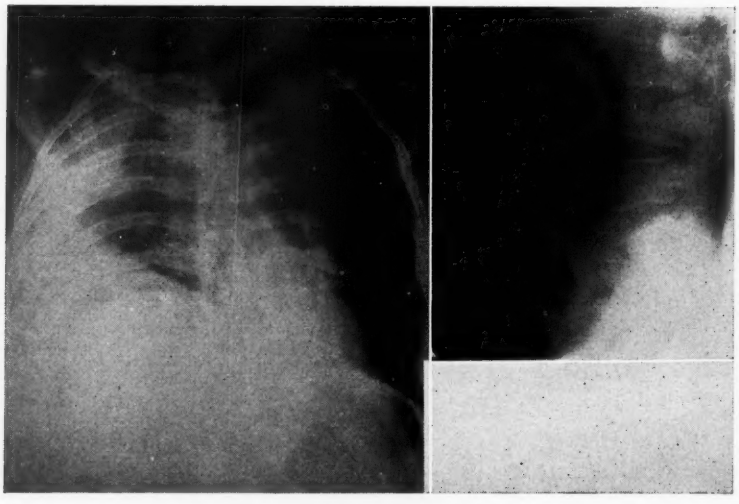

Fig. 4.—Age—29. Year—1957. Etiology—pinned by box-car door. Interval Prior to Hospitalization—6 hours post-trauma. Extent of Diaphragmatic Tear—12 cm. Associated Injuries—laceration of right lobe of liver.

complete and the patients were discharged from the hospital. The convalescence of 1 patient was prolonged because of a concomitant severe head injury which required nearly 6 months of hospitalization.

REVIEW OF THE LITERATURE

The English language literature from 1946 through 1957 was reviewed for case reports which gave sufficient data for tabulation. Many of the papers[1, 6, 11, 16, 26, 27, 31] which appeared during this period speak in generalities

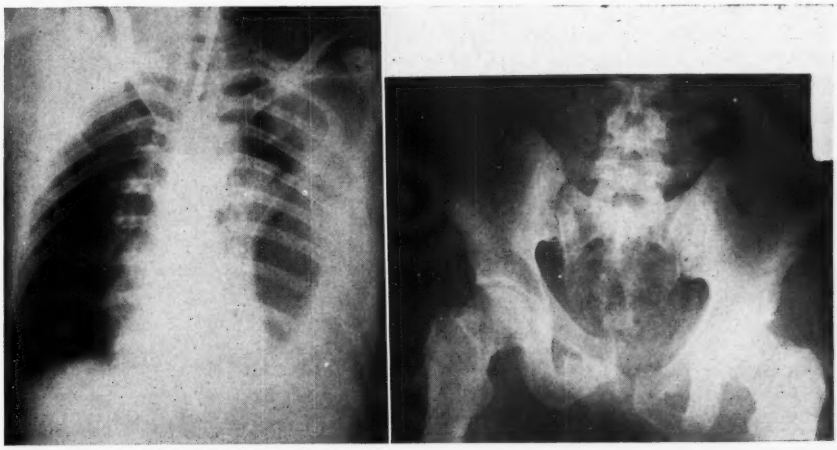

Fig. 5.—Age—43. Year—1957. Etiology—auto crash. Interval Prior to Hospitalization—10 hours post-trauma. Extent of Diaphragmatic Tear—16 cm. Associated Injuries—severe head injury.

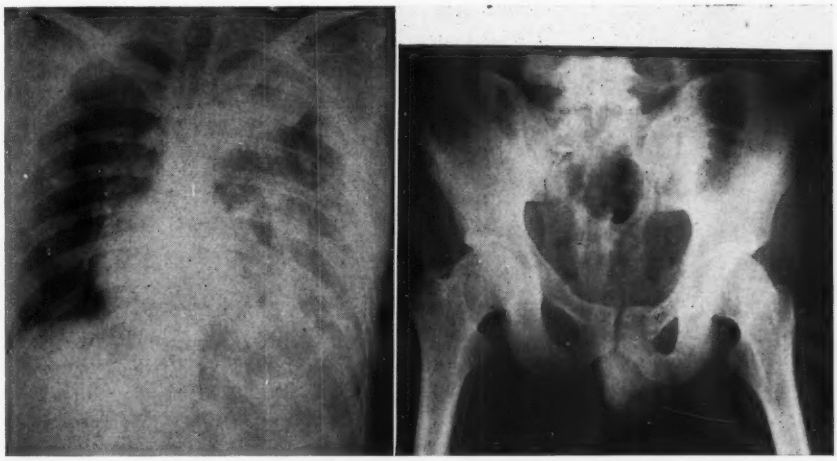

Fig. 6.—Age—24. Year—1957. Etiology—auto crash. Interval Prior to Hospitalization—4 days post-trauma. Extent of Diaphragmatic Tear—12 cm. Associated Injuries—transection of phrenic nerve.

and do not give enough detail to determine the incidence of associated fractures of the bony pelvis or spine. This is unfortunate, for many of these reports contain the largest number of cases. A recapitulation of the findings in the individual case reports, including our own, is listed in Tables I

and II. Evans and Simpson,[19] in 1950, described 5 cases of traumatic rupture of the diaphragm associated with a fractured pelvis in 4 of the cases, 1 of which is reported in the above recapitulation. On the other hand, Lam[36] reported, in 1950, that at the Henry Ford Hospital during the previous 10 years an acute traumatic diaphragmatic hernia had been diagnosed only three times, whereas during this same period 206 fractures of the pelvis had been studied. O'Rourke and Jacobson,[45] in 1955, reported that in 7 traumatic diaphragmatic hernias due to indirect trauma, 4 of the patients had an associated fracture of the pelvis. Donald and Clayton,[15] in 1955, stated that a traumatic diaphragmatic hernia should be suspected in all fractures of the lower dorsal and upper lumbar vertebras, particularly when the fracture is due to jackknifing of the patient.

TABLE I. REVIEW OF 99 CASES OF DEHISCENCE OF THE DIAPHRAGM DUE TO NONPENETRATING TRAUMA (1946-1957)

Etiology		
Motor vehicles		77
Automobile accidents	59	
Run over by car	8	
Hit by car	8	
Motorcycle accident	2	
Industrial and agricultural accidents		7
Mining accidents		5
Falls		5
Miscellaneous causes		5
		99
Associated Fractures		
Pelvis	29	
Spine	11	
	40 (36 patients)	
Side of Dehiscence		
Right	15	
Left	85	
	100 (One bilateral lesion)	
Mortality		
16%		

In 77 of the 99 cases, an automobile or motorcycle was involved. Industrial, agricultural, and mining accidents accounted for 12 of the total number. The left diaphragm was involved in 85 patients, the right in 15, including 1 patient who received a bilateral injury.[39] Fractures of the bony pelvis and spine were found in 36 patients, an incidence of 36 per cent. Rib fractures were described in 26 per cent of the cases reported. This may be due to a failure to report isolated rib fractures.

Serious concomitant visceral injury, chiefly to the spleen but involving nearly all of the intraperitoneal organs, was found in 22 patients. In an additional 7 patients, evidence of vascular insufficiency of the bowel was present at operation. Although 5 of these patients were operated upon from 6 months to 23 years following the injury, vascular insufficiency was found in

TABLE II. REVIEW OF 99 CASES OF DEHISCENCE OF THE DIAPHRAGM DUE TO NONPENETRATING TRAUMA (1946-1957)

Visceral Injury		
Spleen	14	
Stomach	6	
Liver	2	
Small bowel	1	
Urinary bladder	1	
Kidney	1	
Pancreas	1	
	26	(22 patients)
Vascular Insufficiency		
Stomach	3	
Small bowel	3	
Colon	1	
	7	
Obstruction Without Gangrene		
Stomach	7	
Colon	2	
Small bowel	1	
	10	(9 patients)

2 at 39 hours and 11 days following injury. Acute intestinal obstruction without gangrene was found in 9 patients, 1 at 3 days, another at 1 month, and in the remaining 7 from 10 weeks to 17 years following the injury. Thus, 26 per cent of the patients required early surgical intervention, while 38 patients experienced complications either immediately or later which required emergency operation. The over-all mortality in the collected series was 16 per cent.

SUMMARY AND CONCLUSIONS

1. Nine cases of acute dehiscence of the diaphragm associated with nonpenetrating trauma to the chest or abdomen are reported during the period of 1946 through 1957. Six of these cases had an associated fracture of the pelvis and/or lumbar spine.

2. All cases were explored within 5 hours after admission to the hospital. In 3 cases, injury to intraperitoneal organs was encountered which necessitated early operative intervention. All patients recovered.

3. The English language literature was surveyed during the period covered and 99 cases, including the 9 reported in this paper, were encountered. The over-all mortality rate was 16 per cent. In 36 patients, a fracture of the pelvis and/or lumbar spine was reported.

4. In 26 patients, early surgery was mandatory due to associated intraperitoneal visceral injury, vascular insufficiency of the bowel, or complete gastric or intestinal obstruction without gangrene.

5. Early and late complications requiring emergency surgical intervention were found in 38 patients.

6. The importance of early diagnosis and early surgical intervention with adequate exploration of the chest and abdomen is stressed.

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IVALON AS A CHEST WALL PROSTHESIS

An Eighteen-Month Follow-Up

Edward A. Fitch, M.D., and John G. Fries, M.D.,** Houston, Texas*

FOLLOW-UP reports on new and controversial surgical methods are essential for their final evaluation. A previous report[5] described the use of compressed polyvinyl formol alcohol sponge (Ivalon) as a prosthesis to fill chest wall defects. It is the purpose here to supplement the information presented in the former report, and to describe the condition of 3 such prostheses after time intervals of 16, 17, and 18 months.

CASE REPORTS

CASE 1.—(Two chest wall prostheses.) A 7-month-old, 15 pound Mexican female infant with bilateral tumors of the tenth ribs was operated upon Aug. 1, 1956. The left tumor was completely excised, and the 6 by 7 cm. defect closed with an Ivalon sheet. This sheet was 2 to 3 mm. thick and of tenfold compression. The pathologic report indicated that the tumor was a chondroma showing marked hyaline degeneration. (This procedure was recorded in a previous report.[5])

The contralateral tumor was completely excised Oct. 3, 1956, leaving a chest wall defect in the costal plane of 6 by 6 cm. A similar sheet of Ivalon was used to repair the defect. The pathologic diagnosis was "rib (resected portion), exostosis (probably osteochondroma)." It was noted that a histologic difference was present in the second lesion as compared to the previously excised lesion. The first specimen contained a large hyalinized fibrotic area which composed the majority of the lesion, whereas the second lesion was largely definite bone.

The baby, at 14 months of age, was admitted Feb. 11, 1957, for treatment of a right middle lobe pneumonia, apparently unrelated to her previous surgery.

When last seen in January, 1958, both operative areas remained well healed (Fig. 1, *A* and *B*). There were indurated areas palpable over the prostheses, but no other evidence of abnormality. Physical development, posture, and the roentgenologic picture were normal (except for the surgical absence of the excised ribs).

CASE 2.—A 22-year-old Negro woman presented herself in clinic in January, 1956, with the complaint of a painful tumefaction over the area of the third left costochondral junction. This had been first noticed about 1 month previously. Chest x-ray studies were normal. The area was explored through a radial incision in the overlying breast on Jan. 18, 1956, and an angulation at the costochondral junction was the only positive finding. A biopsy revealed normal cartilage. The postoperative diagnosis was Tietze's syndrome.

From the Thoracic Surgery Service of Hermann Hospital, Houston, Texas.
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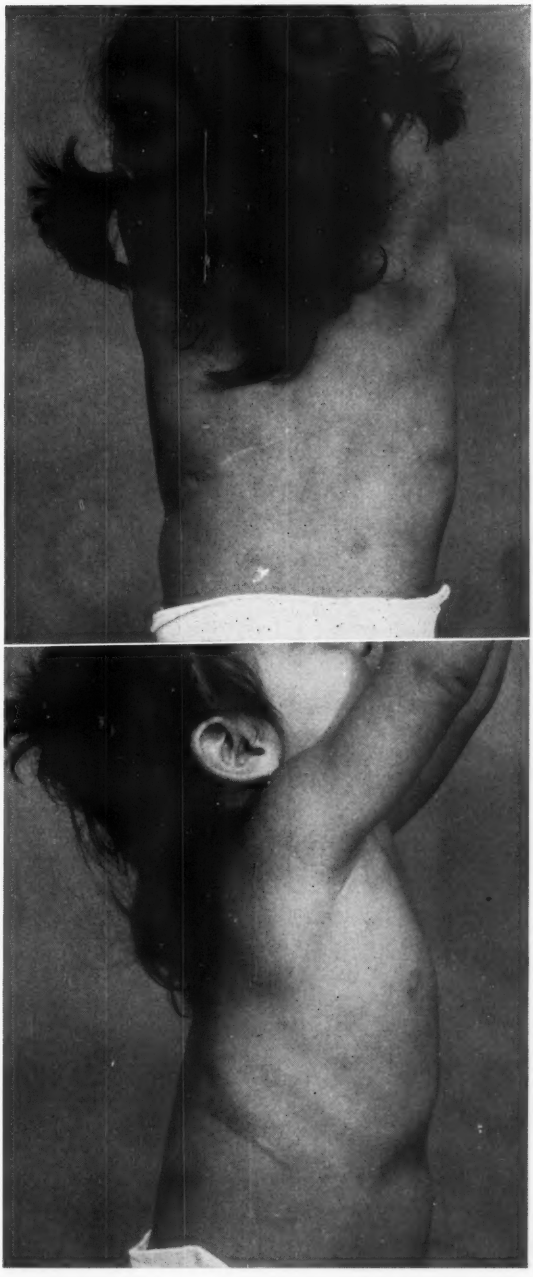
*Formerly Chief Resident in Surgery, Hermann Hospital, Houston, Texas; currently Resident in Thoracic Surgery, Hahnemann Hospital, Philadelphia, Pa.
**Resident in Surgery, Hermann Hospital, Houston, Texas.

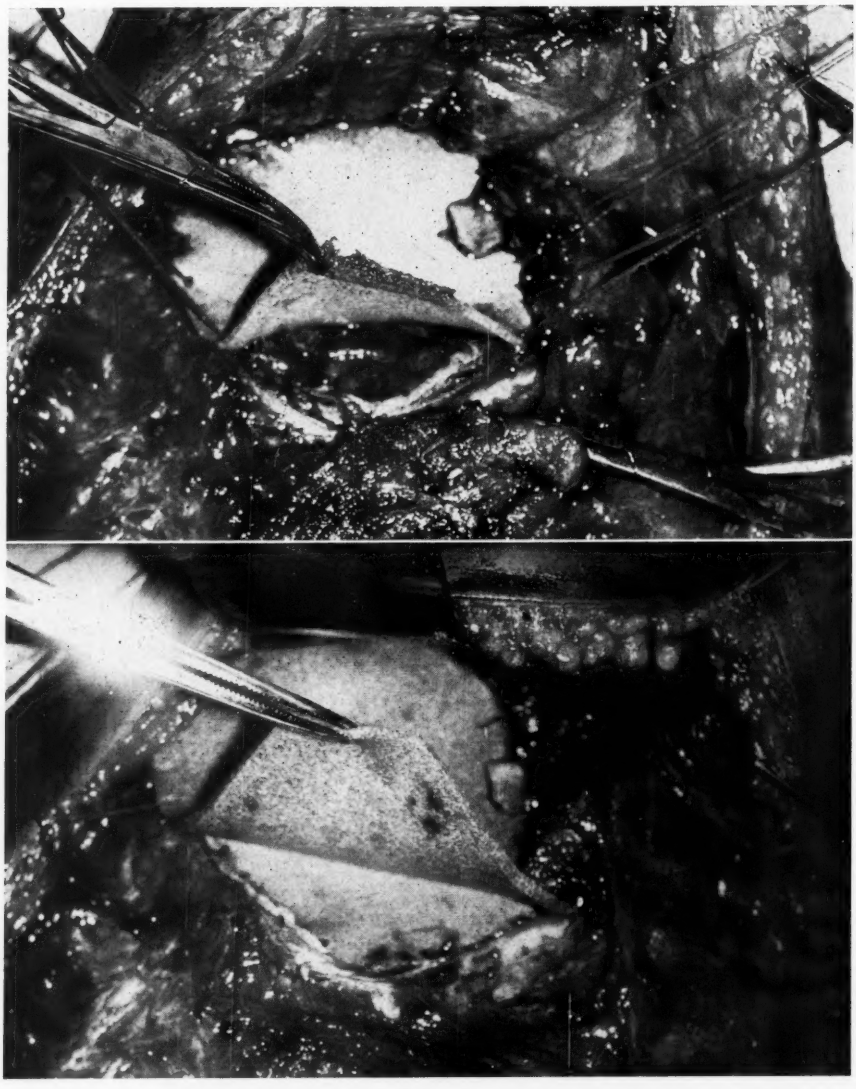


A.

B.

Fig. 1.—*A* and *B*, Case 1. End result in patient with bilateral Ivalon chest wall prostheses.

A.



B.

Fig. 2.—*A* and *B*, Case 2. Two superimposed Ivalon sheets are necessary to provide the necessary stability to repair this chest wall defect.

Fig. 3.—End result in Case 2. The area of the Ivalon prosthesis under the superior scar is firm and stable. Note the tumefaction over the second costochondral junction, which appeared about 10 months postoperatively.

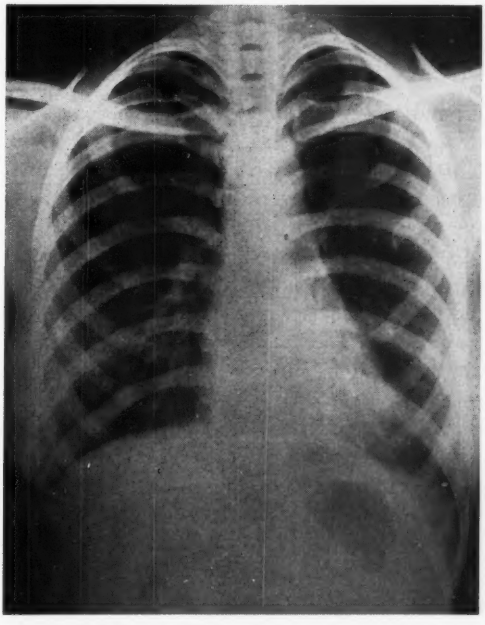


Fig. 4.—X-ray appearance of Case 2, 1 year postoperatively. Note the adsorption of the inferior portion of the second left rib.

The patient continued to complain of pain in the involved area. Serial palpatory examination suggested enlargement of the tumefaction. Since chondroma could not be ruled out, a complete circumferential excision of the involved area was done on April 27, 1956. The approach was through the old operative scar. Examination of the excised specimen revealed no more than an excessively angulated costochondral junction. The histologic examination revealed normal cartilage and bone.

The patient was completely relieved of pain following surgery. However, about 4 months postoperatively, it became evident that a thoracic wall hernia was rapidly developing. A bulge about 8 cm. in diameter would protrude from the chest wall upon straining or coughing. Local discomfort and anxiety were associated with the lesion.

On Sept. 19, 1956, through a submammary breast-reflecting approach, a 9 cm. chest wall defect was exposed. After placing a pleural drainage tube, an Ivalon sheet 2 to 3 mm. thick (compressed tenfold) was sutured to the periphery of the defect. This sheet exhibited a certain amount of fluctuation with extremes of intrathoracic pressure, so a second similar sheet was sutured into place directly overlying the first (Fig. 2, *A* and *B*). This combined prosthesis showed no protrusion or inversion upon being tested by the anesthetist's applied pressure. The wound was closed without superficial drainage.

The postoperative result was ideal until about July, 1957, when the patient first noticed a protrusion over the second costochondral junction (Fig. 3). This has thus far been asymptomatic.

When last seen in January, 1958, the actual area of the prosthesis seemed quite intact. There was no paradoxical movement, and no protrusion upon coughing. There was no pain or tenderness. X-ray studies (Fig. 4) showed the old partially excised third rib, and some adsorption of the inferior margin of the anterior second rib, in the region where the Ivalon prosthesis was attached. The diagnosis would seem again to be Tietze's syndrome, possibly induced by the attaching of the prosthesis to the area.

DISCUSSION

The characteristics of Ivalon have been recorded elsewhere. It would seem appropriate here to take issue with certain previous statements. Recent evidence would indicate that perhaps Ivalon does not "become strengthened as host tissue grows into its interstices."[6] An unknown percentage of Ivalon arterial grafts have shown thinning, dilatation, aneurysm formation, and rupture.[3] Whether or not this deterioration occurs in sheet grafts such as in these chest wall prostheses is unknown at present. Although there is no evidence indicating that Ivalon is carcinogenic, it would not seem prudent to so state this at present.[1, 2, 5] The variability of tissue reaction to Ivalon would seem to place it in the category of substances which may be either accepted, sequestrated, or rejected by the body. Szilagyi and associates[7] designate these responses as Types I, II, and III reaction, respectively. In our experience, the Type I reaction has been predominant.

Ivalon is so conveniently handled that it seemed appropriate to make an effort to overcome its tendency to weaken within the body. Recently we have incorporated stronger fabrics between two fused sheets of Ivalon. Such a patch has recently been constructed of a Teflon net incorporated within a compressed Ivalon sheet, and used to repair a tangential defect in the intrapericardial ascending aorta.[4] Although the patient is now only 3 months postoperative, certainly this extreme test of strength and host adaptability gives early encouraging results. Perhaps such a modification is also applicable in chest wall prostheses.

SUMMARY

A follow-up report is presented of 3 Ivalon prostheses used to repair chest wall defects. Satisfactory results are evident up to 18 months postoperatively.

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THE USE OF CONVOLUTED DISCS IN THE ROTATING DISC OXYGENATOR

Earle B. Kay, M.D., John E. Galajda, B.S., Andrew Lux, M.S., and F. S. Cross, M.D., Cleveland, Ohio

THE ROTATING disc oxygenator* has been used by us in over 147 patients during total cardiopulmonary bypass. This oxygenator has proved itself to be an effective, safe means of oxygenating blood without the danger of air embolism or excessive destruction of blood elements. In no instance has the oxygenator been a factor in producing complications or mortality. There has been an over-all mortality of 22 per cent which has been reduced to 10 per cent in the last 50 patients.

Although the oxygenating capacity of the 20-inch oxygenator with 94 discs at 120 r.p.m. has appeared adequate in the past to fulfill the oxygen needs during total body perfusion in adults, it has appeared that the oxygenating potential or reserve might be increased for large adults. The arterial oxygen saturation in children with the 13-inch oxygenator with 60 discs has varied from 97 to 103 per cent saturation with oxygen tensions ranging from 120 to 400 mm. Hg. In no instance in this range has there been any evidence of oxygen intoxication.

TABLE I. OXYGEN LEVEL IN ADULTS
(20-INCH OXYGENATOR—94 DISCS—120 R.P.M.)

WEIGHT (LB.)	FLOW RATE C.C./KG./MIN.	C.C. FLOW/MIN.	PER CENT SATURATION (TOWARD END OF PERFUSION) ARTERIAL	PER CENT SATURATION (TOWARD END OF PERFUSION) VENOUS	OXYGEN TENSION
Flat Discs					
Range 117-172	40-50	2,500-3,300	84-100	45-71	80-180
Average 144	46.1	2,968	92.1	57.2	119
Convoluted Discs					
Range 106-183	40-50	2,250-3,650	91-105	58-94	160-230
Average 127	47	2,800	98	70	200

As noted in Table I, the oxygen saturation and tension level in adults has been lower. The arterial oxygen saturation has ranged from 84 to 100 per cent with an average of 92.1, while the venous saturation ranged from 45 to 71 per cent with an average of 57.2 per cent. Similarly, the oxygen tension has ranged from 80 to 180 mm. Hg, with an average of 119 mm. Hg. Although this level

From the Department of Research, St. Vincent Charity Hospital, Cleveland, Ohio.
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of oxygenation has not shown itself to be deleterious, it has been felt that in very large individuals it would be desirable to have the margin of oxygenating reserve greater.

Initial experiments were hampered in determining the oxygen capacities of larger rotating disc oxygenators because their oxygenating capacities were always greater than the requirements of a laboratory animal. We now employ in the laboratory an oxygenator larger than the one to be tested—referred to as the de-oxygenator—through which nitrous oxide is circulated to de-oxygenate the blood. This is placed in the same circuit as the oxygenator with intervening pumps. The oxygen tension of both the arterial and venous sides of the oxygenator and de-oxygenator are monitored (Fig. 1).

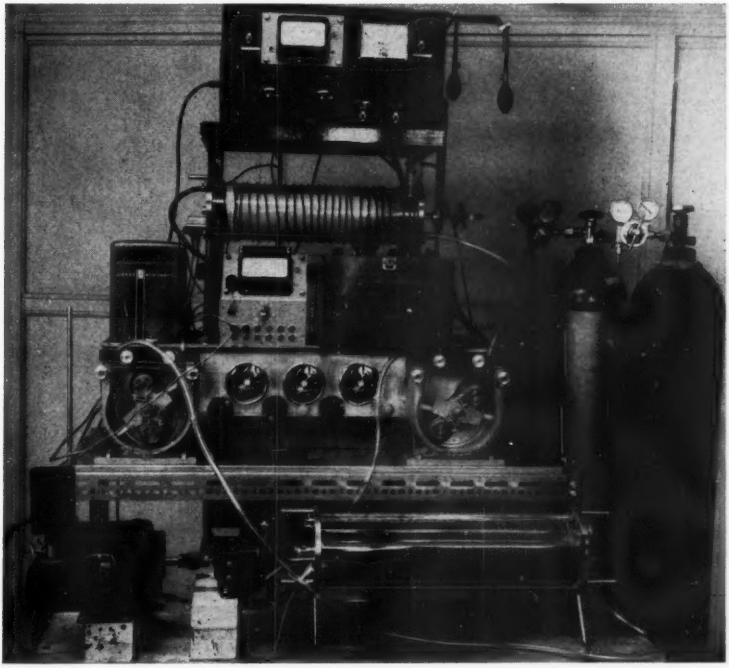


Fig. 1.—Laboratory arrangement for testing the oxygenating capacities of oxygenators by employing a de-oxygenator through which carbon dioxide is circulated to de-oxygenate the blood.

The first and simplest method to increase oxygenating capacity was to increase the oxygenating surface area by increasing the revolutions per minute of the discs from 120 as originally recommended, through varying speeds up to 140 r.p.m. per minute. With the use of the $\frac{3}{16}$-inch spacers between discs, no significant columning of blood occurred with the greater speeds. This maneuver alone in the 20-inch oxygenator containing 94 discs increased the effective oxygenating surface from 148 M.^{2} to 172.2 M.^{2}.

A second method to increase the oxygenating surface was to increase the length of the oxygenator and the number of discs employed. This effects such an increase in oxygenating surface but also increases the amount of the priming volume of the blood, and also has the disadvantage of slowing up the progress of the passage of blood through the oxygenator so that large outputs are more difficult to obtain. This latter factor, however, can again be minimized by increasing the space between the bottom of the cylinder and the rotating discs. However, if this distance is too great, then channeling of blood occurs along the bottom of the cylinder which may not be maximally oxygenated. This

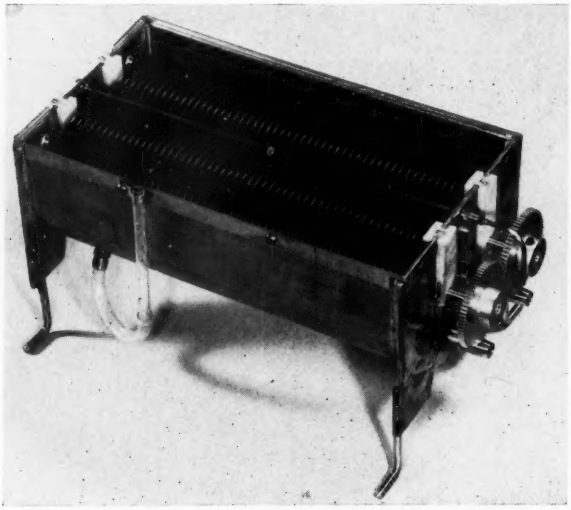
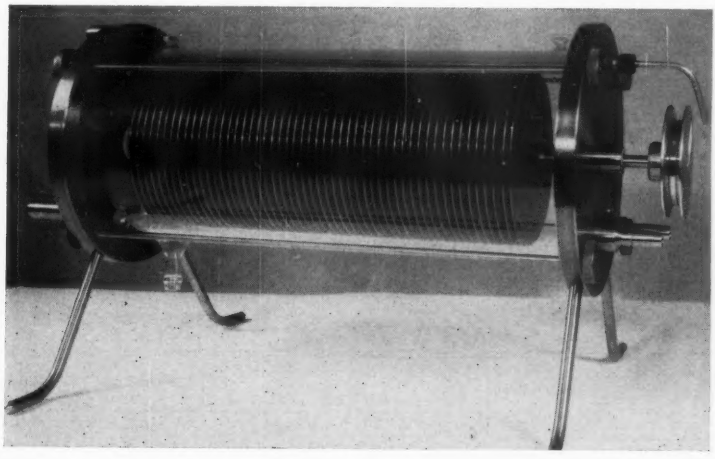


Fig. 2.—The parallel axial oxygenator employed two rows of interdigitating discs.

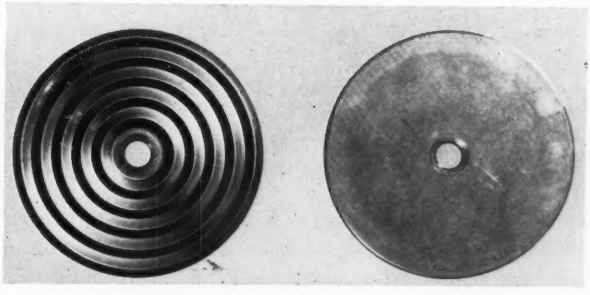
principle was utilized in going from the infant oxygenator with 60 discs to the adult one with 94 discs. The length of the oxygenator could undoubtedly be increased to 25 inches with the addition of another 22 discs, which would increase the free oxygenating surface to 183 M.^{2} per minute, at 120 r.p.m. However, it is felt that the present 20-inch oxygenator is probably the optimal length and size.

A third method was to increase the diameter of the discs. An oxygenator was developed in which the transverse diameter of the discs was increased from $4\frac{3}{16}$ inches to $5\frac{47}{64}$ inches. The length of the oxygenator was also increased to 21 inches with 96 discs. This increased the oxygenating surface area to 187 M.^{2}. However, it also increased the priming volume from 2,800 c.c. to 4,000 c.c. which was felt to be unwise. This oxygenator was used in a patient weighing 180 pounds with a tetralogy of Fallot. The arterial oxygen saturation in this patient was 96 per cent with a venous saturation of 62 per cent at a blood flow of 40 c.c. per kilogram per minute and a total flow of 3,300 c.c.

A fourth method was to use two oxygenators in parallel, connected at the ends by Y-connectors. This is also an effective means of increasing the oxygenating capacity of the oxygenator but has the disadvantage of doubling the priming volume and also requiring the operator to watch both oxygenators simultaneously. To overcome this latter obstacle, a twin unit was designed utilizing two disc units in parallel which partially interdigitated (Fig. 2).



A.



B. *C.*

Fig. 3.—*A*, The 20-inch rotating disc oxygenator. *B*, The stainless steel convoluted disc demonstrating the increased surface area. *C*, The original flat disc.

Each series of discs revolve upward at the center. A metal container was fashioned as noted, because of the difficulty of moulding a double Pyrex cylinder. This unit has a priming volume of 3,400 c.c., contains two units of 50 and 51 discs each, and has a total oxygenating surface of 157 M.^{2} per minute at 120 r.p.m. This is a very effective oxygenator but has the disadvantage of lessened visualization of the oxygenating mechanism by the operator while running, not only because of the metal container but because of the superimposed set of discs.

The most effective method so far devised to increase the oxygenating area, without increasing the priming volume or changing the otherwise desirable features, has been the development of convoluted discs (Fig. 3). These discs are stamped with 90-degree impressions in a concentric manner. This increases the oxygenating surface area per disc 41.4 per cent over the flat discs. In the 20-inch adult oxygenator with 94 discs revolving at 120 r.p.m., the effective oxygenating area of the convoluted discs is 208 M.^{2} per minute, as compared to 148 M.^{2} for the flat discs. In the laboratory the oxygenating capacity of the convoluted discs has been found to be 30 per cent greater than the flat discs.

The convoluted discs have now been employed in 10 adult patients (Table I) with arterial oxygen saturation levels approaching 100 per cent and oxygen tensions of 200 or better. It appears to date that this is the most satisfactory method of increasing oxygenating capacity and reserve without losing any of the other desirable features of the original rotating disc oxygenator.

The comparable free area for oxygenation in these various types of oxygenators is noted in Table II. It is seen that the use of convoluted discs not only effectively increases the oxygenating surface over the flat discs in the 20-

TABLE II. COMPARABLE FREE OXYGENATING AREA

	PRIME VOLUME IN LITERS	FREE AREA FOR OXYGENATING		FREE AREA PER 1,000 C.C. PRIME VOLUME	
		AT 120 R.P.M.	AT 140 R.P.M.	AT 120 R.P.M.	AT 140 R.P.M.
1. 20-inch oxygenator 94 convoluted discs 41 3/16 inch diam.	2.8	208 M.^{2}/min.*	243.6 M.^{2}/min.	74.0 M.^{2}/ml.	86.0 M.^{2}/ml.
2. 20-inch oxygenator 94 flat discs	2.8	148 M.^{2}/min.	172.2 M.^{2}/min.	52.6 M.^{2}/ml.	61.4 M.^{2}/ml.
3. Parallel axial oxygenator 101 flat discs	3.4	157 M^2/min.	184.0 M.^{2}/min.	52.6 M.^{2}/ml.	61.4 M.^{2}/ml.
4. 21-inch oxygenator 96 flat discs 54 7/64 inch diam.	4.0	187 M.^{2}/min. at 97 r.p.m.†	218.0 M.^{2}/min. at 113 r.p.m.†	46.7 M.^{2}/ml.	54.5 M.^{2}/ml.

*Meters squared.
†Comparable to the greater span of the smaller diameter discs.

inch oxygenator by 41.4 per cent but also is the most efficient oxygenating mechanism per 1,000 c.c. volume prime, while retaining the other optimal features of the 20-inch oxygenator. It might appear that convoluted discs would be more traumatic to the blood than flat discs. The factor of hemolysis, which has never been a problem with the use of the rotating disc oxygenator, has even been lowered with convoluted discs and has averaged an increase of only 28 mg. per cent in the patients in whom the convoluted discs have been used.

The results in the use of the convoluted discs have been so satisfactory that they are now being used routinely in the 13-inch oxygenator for children. It has been possible as a result of their oxygenating efficiency to lower the revolutions per minute and in turn the trauma to the blood when the monitoring of oxygen tension by the oxygen electrode indicates tensions in excess of 200 mm. Hg.

SUMMARY

The maximum oxygenating capacity of the 20-inch rotating disc oxygenator has been discussed in its use in adult patients. Various changes have been described in which the free oxygenating surface can be increased without affecting the other desirable features of this oxygenator. Of all such changes tested, the development and use of convoluted discs as described in the text appears to be the most effective means of increasing the oxygenating capacity. This improvement in the oxygenator now adequately fulfills all requirements for oxygen needs in any size individual.

ADDENDUM

Over 200 patients have now been operated upon using the rotating disc oxygenator. The opinions relative to this oxygenator are still similar to those expressed in the article.

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MANAGEMENT OF OUTFLOW TRACT TEAR DURING BROCK PROCEDURE FOR PULMONARY VALVAR STENOSIS

Gilbert S. Campbell, M.D., and Richard L. Varco, M.D.,
Minneapolis, Minn.

IT IS NOT the purpose of this report to debate the relative virtues of the open as opposed to the closed operative approach in the treatment of patients with pulmonic stenosis. Instead, we wish to present one means of salvaging the situation when the posterior wall of the right ventricular outflow tract has been ruptured while utilizing the closed approach.

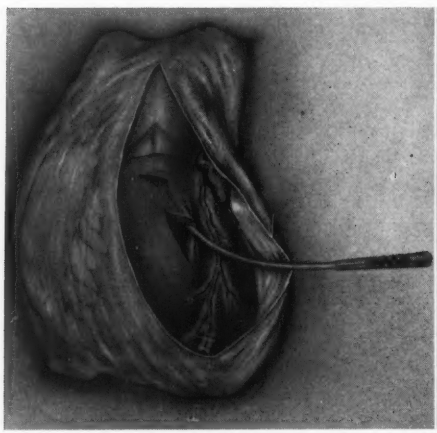

Fig. 1.

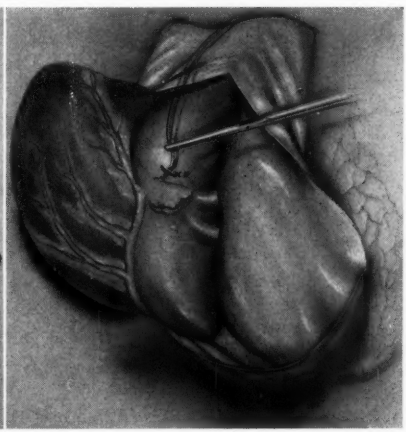

Fig. 2.

Fig. 1.—Production of tear in right ventricular outflow tract.
Fig. 2.—Deliberate dislocation of heart in order to gain exposure for closure of tear.

In any surgical training center, the resident staff learns technical surgery by observing, assisting, and finally doing the various operative procedures. When one takes a resident as far as the "doing" stage with the Brock technique, the resident's first solo into the right ventricular outflow tract may or may not be a smooth one. Approximately once yearly for the past 3 years, this first attempt has resulted in inadvertent puncturing of the relatively inaccessible posterior part of the outflow tract, although it is taught that blind

Department of Surgery, University of Minnesota Medical School, Minneapolis 14, Minnesota.
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instrumentation in the outflow tract is safer when one keeps to the anterior area of the infundibulum and pulmonary artery. In fact, the blunt tip of the bistoury can be palpated through the anterior wall of the main pulmonary artery before it engages with the stenotic orifice in the pulmonary valve. However, if the surgeon encounters resistance in the posterior area of the infundibulum and then unwisely tries to force the instrument past this obstruction, a direct cut or disruptive tear may be produced (Fig. 1). So far, we have found this tear proximal to the pulmonary valve obstruction and hence hemorrhage from the hypertrophied right ventricular cavity has been profuse. Packing the transverse sinus limits, but does not control, the leak. We have found it necessary deliberately to dislocate the heart from the pericardial sac, i.e., to rotate and displace the heart upward and to the right in order to gain access to the tear. The associated hemorrhage, depressed myocardial perfusion and, finally, interference with venous inflow as a result of torsion of the inflow tract can lead to cardiac arrest or ventricular fibrillation. However, only by rotating and displacing the heart can one clearly visualize the rupture in the outflow tract. This hole can then be sutured readily with such exposure (Fig. 2). In one case, a portion of the left auricular appendage was used to buttress an especially large and ragged tear. Cardiac resuscitation was possible in all 3 patients after the tear was closed, and the Brock procedure was subsequently completed in each at the same operation. Functional restoration depends upon the relief of the pulmonic stenosis, and survival with relief of symptoms was obtained in all 3 patients.

AN IMPROVED RETRACTOR FOR THE TRANSVERSE STERNOTOMY

Donald G. McQuarrie, M.D., and C. Walton Lillehei, M.D.,
Minneapolis, Minn.

THE ADVENT of open cardiac surgery has made wide exposure of the entire heart a frequent necessity. A bilateral thoracotomy in the area of the fourth and fifth ribs, coupled with a transverse sternotomy, has proved to be a consistently useful incision. The usual "straight-across" incision in the bone has been modified to a sternotomy cut in a "V" with the apex upward. This makes possible a repair with greater lateral stability, and the more firm apposition of the sternal fragments reduces the incidence of malunion. In adult patients, a heavy duty retractor is required with construction directed specifically toward accommodation to this modification of the transverse sternotomy. This need for a sternotomy retractor was recognized by Pontius and Cooley[1] who have designed a fixed-blade retractor for the "straight-across" sternotomy.

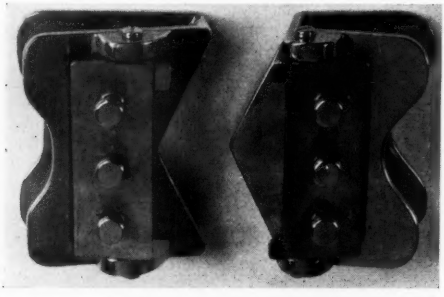

Fig. 1.—A top view of the detachable blades illustrating the V-notch shape and hinge construction for variation in angle.

In designing this retractor the following factors were considered: (1) the need for a strong retractor to achieve adequate spread with a minimum of impedance to exposure, (2) the retractor must be self-retaining, (3) there should be no slippage of the retractor once placed, (4) as the sternum is spread apart the divided ends angulate upward, therefore, the retractor

From the Department of Surgery and Variety Club Heart Hospital, University of Minnesota Medical School, Minneapolis, Minn.

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blades, unless hinged, will ride upward as well, creating an unwieldly obstacle to optimum exposure, and (5) the retractor blades should fit the V-notched sternum.

To encompass these considerations, detachable retractor blades were designed to be adaptable to the Burford-Finochietto self-retaining rib spreader. The upper and lower blades were shaped to fit the respective sides of the V-shaped sternotomy. This gave minimal impingement upon the exposure area.

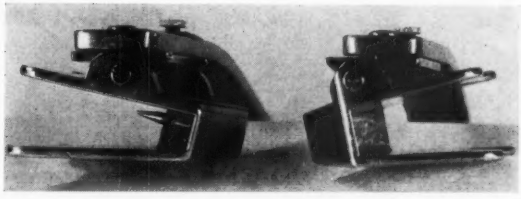


Fig. 2.—A lateral view of the blades showing them attached to the Burford-Finochietto rib spreader. Note the angle of the upper and lower plates of each blade which engage sternal fragments firmly.

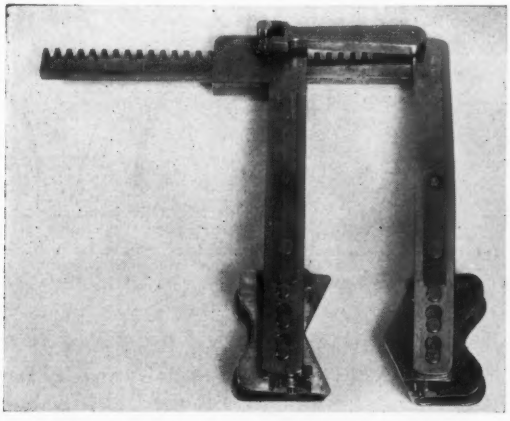


Fig. 3.—An over-all view of the retractor. Its heavy duty construction permits wide exposure with minimal infringement upon working space.

Three sharpened points were placed at the apex of each blade to engage the marrow cavity of the sternum, giving added stability. The blades were hinged in a horizontal plane to accommodate variations in the angulation of the sternal fragments with differences in patient size, incision, and degree of separation of the divided sternal segments. The ability to vary the angle also speeds and facilitates initial placement of the retractor. Stops are placed on the retractor hinges to prevent angulation beyond 40 degrees. The upper and lower plates of each blade are spaced to grasp the rib cage and sternum firmly to prevent vertical displacement. The blades were made from heavy gauge stainless steel.

These retractor blades have been used with excellent success in our adult patients undergoing cardiac surgery via a bilateral sternum-transecting thoracotomy. In this experience one of the principal improvements in design over pre-existing, self-retaining sternal retractors has been the hinging of the blades which facilitates exposure by allowing the arms and body of the retractor to lie flat and out of the way as the sternal segments are spread apart. •

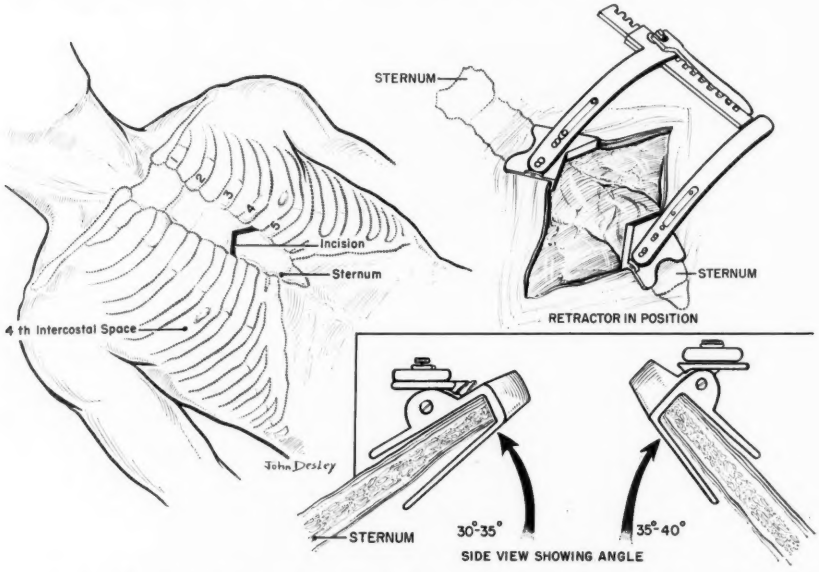


Fig. 4.—The type of "V" sternotomy is illustrated. The wide retraction and fitting of the retractor to the sternal fragments allows maximum exposure. Hinging of the blades allows the body of the retractor to lie flat and out of the way despite variable angulation of the sternal fragments.

REFERENCE

1. Pontius, R. G., and Cooley, D. A.: A Modified Sternal Retractor for Bilateral Anterior Thoracotomy, J. THORACIC SURG. 34: 135-136, 1957.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Thirty-ninth Annual Meeting of the American Association for Thoracic Surgery will be held April 21, 22, and 23, 1959, in Los Angeles, California. Headquarters will be the Hotel Statler.

Requests for Hotel Reservations

These should be mailed directly to Mr. William Truman, Reservation Manager, Hotel Statler, Los Angeles, California. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere in Los Angeles, please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1959 meeting *must be received on or before November 15, 1958,* otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, Suite 308, Carondelet Building, 7730 Carondelet Avenue, St. Louis 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC SURGERY.

MOTION PICTURE SESSION.—Plans are again being made to show suitable motion pictures selected on a competitive basis. *The films themselves,* together with descriptive material concerning length of presentation, etc., must be received by Dr. John C. Jones, Suite 509, 1136 West Sixth Street, Los Angeles 17, California, *before November 15, 1958.*

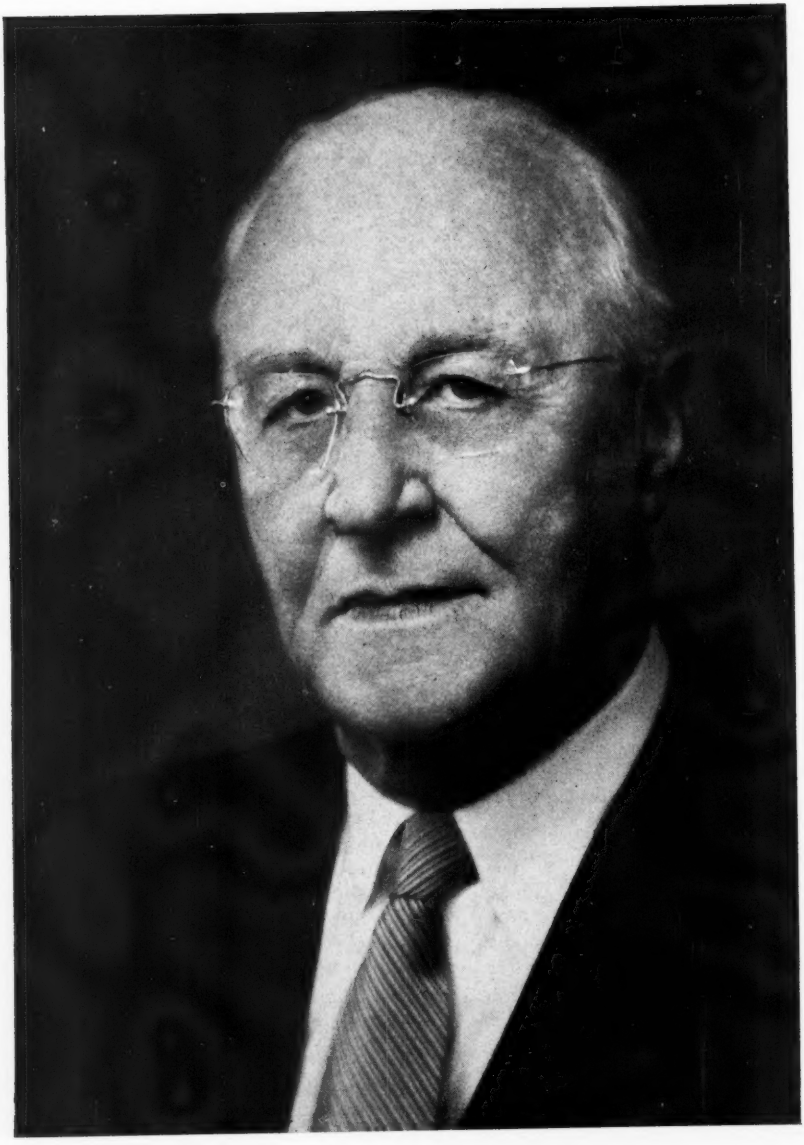
Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than November 15, 1958,* otherwise the application will be deferred for consideration until the 1960 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Dr. Duane Carr
Chairman of the Membership Committee
899 Madison Avenue
Memphis 3, Tennessee

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*



Evarts A. Graham